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American Journal of Diseases of Children

VOLUME 39 MARCH, 1930 NUMBER 3

THE DETERMINATION AND REGULATION OF BLOOD CLOTTING FUNCTION IN CHILDHOOD *

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NEW YORK

Hemorrhagic diatheses in childhood constitute a variety of disorders with a common tendency to bleed. They may be manifested in the form of petechial spots, purpuric extravasations or ordinary loss of blood from free surfaces. These clinical expressions of a disorder of the blood represent active hemorrhagic disease in all grades of severity. But there is a comparable group of disturbances of the blood in which a tendency to bleed or clot representing potential hemorrhagic disease may be precipitated by a sudden change in the vascular system. These latent aspects of hemorrhagic disease have thus far been neglected.

Hemorrhagic disease, latent or active, results from an alteration in either the vascular system or its blood content. An understanding of the mechanism must be based first on knowledge of the normal formative tissue. The reticulo-endothelium is the common hematopoietic tissue which is capable of giving rise to different varieties of blood cells and blood content in various environments. The developmental history of the reticulo-endothelium and that of ordinary vascular endothelium are similar, but in postnatal life their structures and functions appear separate. Even if there are places in which the former performs the function of bounding vascular spaces, as in the splenic pulp, it only complicates the correlation of the clinical entities of hemorrhagic disease.

Fundamental discrepancies in the views of hematologists as to the embryonic nature of the blood-forming tissues throughout their whole life history challenge, for the present, further classification of the problems of bleeding. Though the hematopoietic tissues undergo deep-seated changes in hemorrhagic disease and though alterations in the

* Submitted for publication, Nov. 18, 1929.

* From the Departments of Pediatrics and Surgery of the Fifth Avenue Hospital.

components of the blood are symptomatic, we have nevertheless approached the problem from the latter standpoint.

Ten years ago, one of the authors (I. N. K.) began in Bordet's laboratory a series of studies on the mechanism of coagulation of the blood from the physicochemical standpoint.[1] This necessitated the use of standard reproducible clotting systems attained by combining the few components sufficient for the complete phenomenon of coagulation. These results have convinced us that clinically hemorrhagic disease could be characterized by the variation in these blood substances. Such knowledge might provide a more substantial basis for the early recognition, prevention and treatment of hemorrhagic disease.

Quantitative studies of the clotting factors were made routinely on about 400 patients admitted to the surgical and pediatric services of the hospital. The present report includes only the studies of cases of hemorrhagic disturbances in childhood, based on the following tests: (1) the prothrombin index; (2) the antithrombin index; (3) the degree

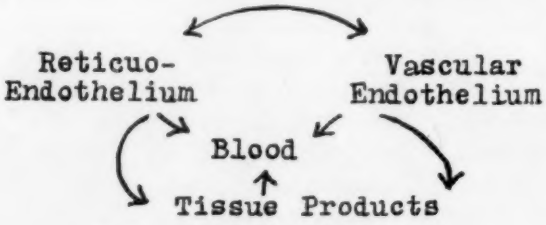


Fig. 1.—The blood-formation cycle.

of platelet disintegration; (4) the platelet count; (5) the fibrinogen content; (6) the calculated index of blood clotting function, and (7) the bleeding and clotting time.

THE MECHANISM OF CLOTTING—THE COMPONENTS INVOLVED IN COAGULATION OF THE BLOOD

Physicochemical studies reveal that blood plasma, as long as its constituents are not dissociated by extraneous forces, is a single complex in equilibrium rather than a mixture of substances. The initial views of Harvey (1653) and of Woodbridge (1886) have come into their own again: "Blood plasma is protoplasm and clotting is the last act of living blood."

Blood, when shed, exhibits the striking physiologic function of dissociating into the components necessary for the clotting reaction. The clotting function of the blood then depends (1) on the degree of

1. Kugelmass, I. Newton: Arch. internat. de physiol. **21**:139, 1923; Colloid-Chemistry, Monograph, McGraw-Hill Book Company, New York, 1925, vol. 111, pp. 158-207.

dissociation of plasma (the incubation period of clotting) and (2) on the liberation of certain substances in sufficient concentration to form a gel (the actual clotting). The dissociation of shed blood adequate to yield a clot is a determining preclot function. A graphic presentation of this process would be as shown in figure 2.

EVALUATION OF THE CLOTTING FUNCTION OF THE BLOOD IN CHILDHOOD

The quantitative determination of the dissociated compounds involved in coagulation of the blood offers a basis for evaluating the clotting function of the blood. And the value of each of the clotting substances of a patient gives us an insight into the nature of the clotting deficiency and hence the hemorrhagic status of the child. All the determinations given below may be carried out in an hour.

Value of Clotting Time.—The clotting time of the blood is essential, but not conclusive in determining the hemorrhagic tendency of a patient. The clotting time may be normal, though spontaneous bleeding is present, i. e., in purpura and jaundice; and clotting may be delayed, though there is no hemorrhage.

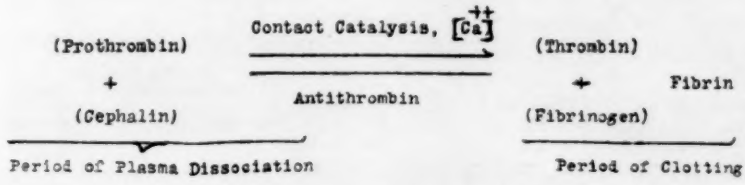


Fig. 2.—The clotting mechanism.

The determination of the clotting time of the blood passing through skin is no criterion of the true clotting status of blood, and hence no indication of what might be expected in the field of operation in other tissue. All injured tissues, as well as blood when shed, dissociate into substances conducive to their coagulation. This contributory factor of the tissue may be eliminated by taking the clotting time by venipuncture.

Determination of Clotting Time (Venipuncture).—Draw 1 cc. of blood and transfer to a test tube 8 mm. in diameter (the greater the diameter of the tube, the slower the clotting). Place the tube in a water bath at 38 C. Coagulation is complete when the tube can be inverted without the clot's being displaced (normally in from five to eight minutes).

Determination of Clotting Time (Skin Puncture).—Touch the end of a capillary tube (3 cm. by 0.6 mm.) to the first drop of blood issuing from a stab in the finger or ear. Place in the creases of the palm and cover by closing the hand to maintain a fairly uniform temperature (from 34 to 35 C.). The clot initiation time (latent period) is the first visible departure from fluidity. The clot formation time is the first fibrin thread seen between the ends when the capillary is broken by bits every half minute (normally, in from three to five minutes).

Properties of Antithrombin.—Antithrombin is the substance maintaining the stability of the plasma complex. When blood is shed, the

dissociation of the plasma produces clotting components which, by mass action, decrease the stabilizing effect of the antithrombin. Its content is directly proportional to the colloid stability of the blood. High values of antithrombin indicate a hemorrhagic tendency, and low values indicate accentuated coagulability of the blood.

Antithrombin Index.[2]—Blood obtained by puncture of the skin is drawn into a Wright tube, allowed to clot and then centrifugated; 0.1 cc. of serum is drawn off into a small test tube by means of a capillary pipet and heated in a water bath at 60 C. for ten minutes. (Prothrombin is thus destroyed.) A control blood is carried through the same procedure. The heated serums are cooled and to each is added 0.3 cc. of a prepared solution of thrombin. The tubes are placed in a water bath at 38 C. The antithrombin index is the ratio of the clotting time of the patient's blood to that of the control.

Preparation of Fibrinogen.—Blood from the slaughter house is drawn into a vessel containing sufficient sodium citrate to give a final concentration of 0.5 per cent. The plasma is collected by centrifugation, and to each 25 cc. is added 4 Gm. of sodium chloride. The precipitated fibrinogen is collected, washed several times in 15 per cent sodium chloride containing 0.5 per cent sodium citrate and finally dissolved in 25 cc. of 0.5 per cent sodium citrate.

TABLE 1.—*Antithrombin Test*

Heated Serum, Cc.	Thrombin, Cc.	Fibrinogen, Cc.	Clotting Time at 38 C. Incubation Time, 15 Minutes	
			Control 5 minutes	Patient +
0.1	0.3	0.5		

Preparation of Thrombin.—Twenty-five cubic centimeters of the plasma collected by the procedure just described, is precipitated by 10 Gm. of ammonium sulphate and filtered by means of a Buchner suction funnel. The ammonium sulphate is expressed as completely as possible to obviate the necessity for dialysis. The precipitate containing the plasma prothrombin may be preserved for weeks as a moist paste. The thrombin solution is prepared by dissolving 0.25 Gm. of the paste in 10 cc. of water, adding 2 cc. of a 0.1 per cent emulsion of cephalin and 2 cc. of 1 per cent solution of $CaCl_26H_2O$. This thrombin solution remains active for several hours.

Properties of Prothrombin.—Prothrombin is a protein substance identified with albumin and globulin and is electro-negative in blood. It acts as a nucleus for the electrical condensation of the clotting components in the formation of a gel. Its concentration is directly proportional to the clotting activity of blood. High values indicate accentuated coagulability of blood, and low values indicate a tendency to bleeding.

Prothrombin Index.[3]—Blood obtained by puncture of the skin is drawn into a Wright tube containing 0.1 cc. of 1 per cent sodium oxalate and centrifugated.

2. Mills, C. A.: Antithrombin Test in Typhoid Fever: Improvements in Technic, Arch. Int. Med. **39**:618 (May) 1927.

3. Howell, W. H.: Harvey Lecture, New York, 1917.

One-tenth cubic centimeter of the plasma is placed in three tubes (6.8 by 1.3 cm., flat bottom) in a water bath at 38 C., and to these are added in series 0.1, 0.2 and 0.3 cc. of 0.5 per cent $CaCl_2 6H_2O$. The shortest clotting time in the series is the prothrombin time. The prothrombin index is the ratio of the clotting time of the control to that of the patient's blood.

Properties of Fibrinogen.—The fibrinogen of body fluids is a globulin formed in the liver and coagulable by thrombin. It constitutes the potential clot structure dispersed in the plasma in the most readily precipitable form. Its transformation into soluble fibrin completes the clotting reaction. High fibrinogen content accelerates clotting and syneresis or retraction of the firm fibrin clot from the gel. Low fibrinogen content gives a nonresistant skein inadequate for retraction in arresting hemorrhage.

Determination of Fibrinogen Value.[4]—Blood is drawn into a tube containing 0.2 cc. of 3.5 per cent sodium citrate and centrifugated under petrolatum. The refractive index of one drop of the plasma at 38 C. is estimated by means of

TABLE 2.—*Prothrombin Test*

Oxalated Plasma, Cc.	0.5 per Cent $CaCl_2$, Cc.	Clotting Time at 38 C.	
		Control 3 minutes	Patient +
0.1	0.1		
0.1	0.2		
0.1	0.3		

a Pulfirish refractometer. One-tenth cubic centimeter of 1.5 per cent $CaCl_2 6H_2O$ is added to the tube to coagulate the fibrinogen, and the mixture is then centrifugated. The refractive index of a drop of the serum is then determined. The percentage of the fibrinogen of the blood is the difference between the index of plasma and that of serum multiplied by the factor 0.187.

Properties of Platelets.—Platelets are lipoidal protoplasmic separations from megakaryocytes in the bone-marrow. They are protein-phospholipin complexes containing 70 per cent protein, 15 per cent lipoids, 5 per cent cholesterol and 5 per cent basic salts. Clotting of blood takes place, other factors being equal, when there is an adequate platelet content and a rapid platelet disintegration, liberating phosphatides. In fact, platelets which do not agglutinate rapidly are functionless for clotting.

Platelet Count.—Draw blood with a pipet for making red blood counts and dilute with 3 per cent citrate (1:200) without adding any stain as a diluting agent. Allow the cell to stand for ten minutes before counting the platelets in the customary counting chamber.

Determination of the Percentage of Platelet Lysis.[5]—Blood is collected in a short paraffined tube, and platelet counts are made at fifteen minute intervals,

4. Kugelmass, I. N.: Compt. rend. Soc. de biol. **87**:802, 1922.
5. Howell, W. H., and Cekada, E. B.: Am. J. Physiol. **78**:500, 1926.

counting only the platelets that are single and not agglutinated into clumps. The platelet lysis percentage is the fraction of the platelets which disintegrates within one hour.

Calculation of the Index of the Clotting Function of the Blood.—Normal blood shows on analysis that the clotting components are contained in fairly constant concentrations. Typical normal values are given in table 3 as representative of determinations made on patients with normal clotting function of the blood.

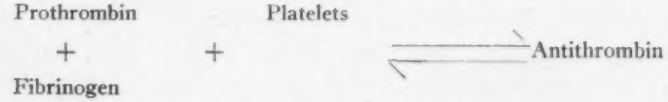
The constancy of the values of the components in clotting of the blood is evident from the data on these patients. The variation in the platelet counts and the platelet disintegration is within the accepted normal range. We have come to believe that high platelet counts are associated with chronic infection. The rate of platelet disintegration at the end of one hour is over 40 per cent, the low normal level.

A composite value of the ability of a blood to clot may be calculated from these determinations. Certain of the blood substances, i. e., pro-

TABLE 3.—*Blood Analyses Indicating Normal Values of the Clotting Components*

Name	Diagnosis	Clotting Time	Bleeding Time	Prothrombin	Fibrinogen, %	Antithrombin	Platelets	Platelet Disintegration, %	Clotting Index
B. F.	Postauricular abscess.....	5'15"	1'30"	1.0	0.56	1.04	240,000	40	0.5
D. B.	Chronic appendicitis.....	3'30"	2'30"	1.0	0.54	1.0	300,000	50	0.5
C. G.	Cystopyelitis.....	4'30"	1'30"	1.0	0.54	1.0	350,000	71	0.5
R. L.	Perineal repair.....	4'15"	2' 0"	1.0	0.60	1.0	225,000	50	0.6
M. C.	Rectovaginal fistula.....	5' 0"	2' 0"	1.0	0.64	1.04	185,000	45	0.6

thrombin, fibrinogen and platelets, tend to favor clotting, and others (antithrombin) tend to reverse this process, i. e., favor bleeding. In this chemical mechanism, the activity for clotting or bleeding is proportional to the concentration of each interactive substance.



Expressing this reaction in terms of the law of mass action, we have

$$\frac{(\text{Prothrombin})\quad(\text{Fibrinogen})\quad(\text{Platelets})}{(\text{Antithrombin})} = I$$

Introducing normal values for these substances, we have

Prothrombin index	= 1
Fibrinogen	= 0.5 per cent
Platelets	= 200,000
Platelet lysis	= 50 per cent in one hour
Active platelets	= 100,000
Antithrombin index	= 1

The normal index of clotting function of blood is therefore 0.5 ± 0.2. Values over 1 indicate a marked tendency to clot, and values below 0.2 indicate a marked tendency to bleed.

The index of clotting function has been a more accurate clinical criterion of the condition of the patient than has hitherto been available by laboratory methods. In certain chronic diseases, however, in which the platelets have been markedly increased, no direct relation has been observed between the unusually high clotting index and the possibly increased coagulability of the blood. We have therefore evaluated the clotting function from the limiting factors:

$$I = \frac{(\text{Prothrombin}) \qquad (\text{Fibrinogen})}{\text{Antithrombin}}$$

The normal index thus becomes 0.5 ± 0.2.

TABLE 4.—*Blood Analyses in Diseases with Altered Clotting Function*

Patient	Diagnosis	Clotting Time	Bleeding Time	Prothrombin	Fibrinogen, %	Antithrombin	Platelets	Platelet Disintegration, %	Clotting Index
	Patients with Marked Tendency to Bleed								
M. L.	Hemophilia	10′ 0″	.....	1.00	0.64	1.11	95,000	15	0.008
B. N.	Hemorrhagic disease of the new-born	11′15″	.....	0.66	0.19	1.5	165,000	20	0.04
S. S.	Hemophilia	5′ 0″	4′ 0″	0.66	0.54	1.57	250,000	24	0.2
B. B.	Nutritional bleeder	4′30″	.....	0.87	0.46	1.25	240,000	62	0.3
	Patients with Marked Tendency of the Blood to Clot								
L. F.	Mesenteric thrombosis	2′30″	1′30″	1.54	0.93	0.75	440,000	67	1.9
G. S.	Gallstones, gastric polyp, complication thrombosis.	3′30″	.....	1.54	0.93	0.75	300.000	50	1.9
O. P.	Cardiac disease with embolus in popliteal artery	3′15″	4′30″	1.7	1.12	0.46	275,000	83	4.1

CLASSIFICATION OF DISEASES WITH ALTERED BLOOD CLOTTING FUNCTION

Abnormal bleeding is a common symptom accompanying truly hemorrhagic diseases on the one hand and the course of many other diseases on the other. However diverse bleeding conditions may be, the excessive loss of blood is due to a decrease in the concentration of the clotting components of the blood or to damage of the vascular system. But equally prevalent are the surgical calamities of thrombosis and embolism heralded without noticeable warning. These conditions, we have come to believe, are due either to an increase in the concentration of the clotting components or to a change in the properties of blood—stasis and increased viscosity.

The classification of hemorrhagic diseases has hitherto been limited to the well defined bleeding conditions—hemophilias and purpuras.

Bulloch [6] characterized hemophilia as an inherited tendency in males to bleed, and Howell [5] found the blood platelets most resistant to lysis, a process of disintegration which is indispensable for clotting. But Frank [7] described purpura as thrombocytopenia with actual deficiency in the total number of platelets.

It is possible to trace in different children, and sometimes in the same child at different times, every grade between purpura hemorrhagica, in which effusions of blood may be large, and purpura simplex, in which they are limited to petechiae. Each of these disorders is characterized by a shortage of the platelets, by a normal coagulability of the blood and by a loss of contractility of the blood clots. There is, then, no distinctive difference, except severity, between these conditions.

TABLE 5.—*Classification of Diseases in Which the Clotting Function of the Blood Is Altered*

Blood clotting function in disease		Disease Groups		Prothrombin	Fibrinogen	Antithrombin	Platelets
	Increased Index > 0.8	Infection	Thrombosis				
			Thrombo-angiitis obliterans	+	..	—	..
			Phlebitis	..	+	..	+
			Pneumonia	+	..	—	+
			Tuberculosis	..	+	..	+
		Metabolic disturbances	Diabetic gangrene	..	..	..	+
			Cholelithiasis	+	+	—	..
			Renal colic	..	+	..	..
			Carcinoma	..	..	..	+
	Normal index = 0.5	Physical conditions	Trauma				
			Congestion				
			Hypertension				
			Surgical wounds				
		Hereditary conditions	Melena neonatorum	—	..	..	Lysis decreased
			Hemophilia				
			Epistaxis				
			Hemoptysis				
		Blood diseases	Secondary anemia				
			Pernicious anemia	—	—	+	..
			Chlorosis	..	..	..	—
			Leukemias	..	..	..	—
	Decreased index > 0.2	Liver diseases	Stenosis of bile duct	+	..	..	—
			Cirrhosis	..	..	..	—
			Jaundice	—	..	..	—
		Infections	Acute infections	..	..	+	—
			Typhoid	..	—	—	—
			Syphilis	..	..	..	—
			Arthritis	..	..	+	..
		Toxic conditions	Purpura	..	..	..	—
			Allergy	—	..	..	—

But a consideration of the problems of bleeding associated with hemophilia or purpura involves only that small group of hemorrhagic disorders in which the deficiency is in the quality of the platelets or in their quantity. The clotting mechanism is affected by substances other

6. Bulloch, W.: Hemophilia, London, 1911.

7. Frank, E.: Berl. klin. Wchnschr. **52**:454, 1915.

than platelets, and hence all hemorrhagic disease, latent or manifest, may provisionally be classified according to the deviation in one or more of the clotting components, and the clotting function gives an integral value of the blood content in clotting components. The classification of diseases given in table 5 is the result of data in 400 cases accumulated in our laboratory.

EVALUATION OF THE CLOTTING FUNCTION OF THE BLOOD BEFORE OPERATION

Routine examination of patients' blood preoperatively and three and five days postoperatively was carried out on the surgical service as

TABLE 6.—*Analysis of the Clotting Components in the Blood of Suspected Bleeders Before Tonsillectomy* *

Patient	Clotting Time	Bleeding Time	Prothrombin	Fibrinogen, %	Antithrombin	Platelets	Platelet Disintegration, %	Clotting Index	Remarks
			Group 1. Patients with Deficient Clotting Function						
S.	5′ 0″	4′ 0″	0.66	0.54	1.57	250,000	24	0.2	Hemophilia
D.	7′30″	2′30″	0.87	0.42	1.08	195,000	21	0.3	Hemophilia
B.	6′45″	2′ 0″	0.13	0.56	6.8	300,000	10	0.003	Hemophilia
L.	.....	.....	0.2	0.64	5.0	.....	8	0.02	Hemophilia
			Group 2. Patients with Normal Clotting Function						
B.	.....	.....	0.87	0.37	1.08	220,000	43	0.3	Tonsillectomy
T.	.....	.....	1.00	0.37	1.00	215,000	48	0.4	Tonsillectomy
E	.....	.....	0.82	0.47	1.07	190,000	47	0.4	
S.	.....	.....	2.00	0.64	1.04	230,000	35	0.6	
F.	4′ 0″	2′ 0″	1.38	0.59	1.00	200,000	25	0.8	Tonsillectomy
K.	8′15″	2′30″	0.96	0.93	0.96	180,000	28	0.9	Tonsillectomy
R.	5′ 0″	.....	1.38	0.74	0.86	180,000	39	1.0	Tonsillectomy
M.	.....	.....	1.54	0.75	0.86	160,000	38	1.3	
			Group 3. Nutritional Bleeders						
H.	6′45″	6′15″	0.6	0.60	1.50	175,000	37	0.1	
	5′45″	.....	0.93	0.64	1.07	150,000	37	0.1	
	6′30″	.....	0.93	0.60	1.07	190,000	37	0.1	
B.	4′30″	.....	0.87	0.46	1.25	240,000	62	0.2	
	8′ 0″	.....	0.93	0.28	1.25	210,000	52	0.2	
S.	.....	.....	0.87	0.28	1.08	340,000	50	0.2	
			0.87	0.54	1.08	345,000	48	0.4	
T.	.....	.....	0.85	0.32	1.07	350,000	30	0.25	
			1.00	0.37	1.00	350,000	31	0.35	

* From the service of W. M. Hunt, Fifth Avenue Hospital.

reported elsewhere.[8] The present data refer to the pediatric service, with special reference to determinations made previous to tonsillectomy. Among the great number of patients undergoing tonsillectomy there is a group on whom operation is undertaken at definite risk and who present difficulties if operation is performed. The clotting time is no index of the clotting function and has been found nonconclusive in an exhaustive study by Hunt.[9] On the other hand, there is another group

8. Bancroft, F. W.; Kugelmass, I. N., and Stanley-Brown, M.: Ann. Surg. **81**:161, 1929.

9. Hunt, W. M.: Ann. Otol. Rhin. & Laryng. **36**:187, 1927.

whose clotting times have been found increased and who are suspected of being bleeders. The results of tests of the clotting function of such patients have been found normal in a number of cases and have thus eliminated the patients in these cases from the category of bleeders.

GROUP 1.—Five patients appeared for an indicated tonsillectomy. The clotting times were normal, and yet the past histories revealed bleeding tendencies from birth. The low percentage of the platelet disintegration characterized such patients as hemophiliacs.

GROUP 2.—Several patients appeared for tonsillectomy with histories of having bled readily on bruising (F. O.), or of having been denied operation at another hospital because of prolonged clotting time (K.), or of having a family history of bleeding (R.). The clotting function determinations were normal, and operation was uneventful in each case.

GROUP 3.—Several patients scheduled for tonsillectomy had histories of bleeding readily. Studies of the clotting function showed that the previous difficulties in arresting bleeding in these patients were due to clotting deficiencies correctable by a clotting diet (see section on Dietary Treatment of Hemorrhagic Diseases).

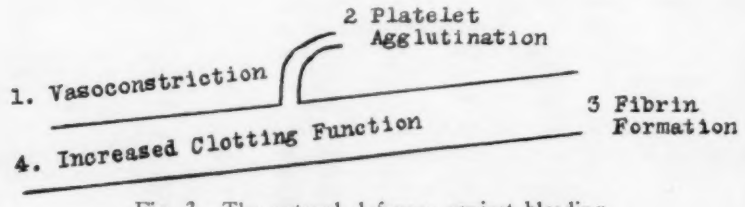


Fig. 3.—The natural defenses against bleeding.

Patient H. showed an index of 0.1 which, when he was on a diet to increase clotting, rose to 0.3 and later to 0.4. The resulting status of this patient's blood was more favorable for operation. B., an intern at the hospital, had an index of 0.2. His tendency to bleed was associated with his vegetarian dietary. He was advised to adopt a diet to increase clotting, but he failed to keep it up, and after operation bled periodically for a week. The clotting index remained 0.2 on a persistent vegetarian regimen.

THE DIETERY TREATMENT FOR HEMORRHAGIC DISEASE

Hemorrhagic manifestations are best controlled by the augmentation of physiologic processes which tend to limit bleeding. The first defense against bleeding is increased vasoconstriction, and this reaction may be accelerated by the application of heat or cold, as well as by epinephrine and hemostats combined. The second natural defense against bleeding is the agglutination of platelets in the orifices of wounded capillaries. The third defense is the clotting of blood in wounds. The fourth defense is the compensatory increase in coagulability of blood following bleeding.

The treatment for hemorrhage by direct action on circulating blood had been attempted in many ways. Coagulant hemostats extracted from

viscera and injected by one route or another have given variable results in view of the lack of standardization of their efficacy. X-ray irradiaction of the splenic area has been found to increase the coagulability of the blood, but the effect lasts only several hours. Widal [10] observed increased coagulability during anaphylaxis, and injections of horse serum, peptone and fibrinogen to induce such a state have since been utilized. But transfusion or subcutaneous injection of compatible blood is most effective in accelerating the clotting function.

But all the natural defenses against bleeding become insufficient if the concentration of the components involved in coagulation of the blood is decreased. While a transfusion of blood is the most effective therapeutic measure, we believe the blood clotting function may be augumented by dietary measures. The chemical nature of the clotting com-

TABLE 7.—*Results of Test Made on Blood (1) After a Normal Diet, (2) After Forty-Eight Hours on a Carbohydrate and Vegetable Diet, (3) After Forty-Eight Hours on a Visceral Protein Dict*

Dog	Diet	Prothrombin	Fibrinogen, %	Antithrombin	Platelets	Index
1	Normal diet	1.11	0.64	1.16	200,000	0.6
	Carbohydrate and vegetable diet	1.11	0.64	1.16	200,000	0.6
	Protein-lipin diet	1.45	1.12	0.95	250,000	1.7
2	Normal diet	1.00	0.54	1.00	400,000	0.5
	Carbohydrate and vegetable diet	0.74	0.54	1.16	220,000	0.3
	Protein-lipin diet	1.00	0.64	0.95	300,000	0.7
3	Normal diet	1.11	0.64	1.16	220,000	0.6
	Carbohydrate and vegetable diet	1.11	0.28	1.00	135,000	0.3
	Protein lipin diet	1.26	0.69	1.00	210,000	0.9
4	Normal diet	1.00	0.40	1.16	200,000	0.3
	Carbohydrate and vegetable diet	1.00	0.40	1.16	525,000	0.3
	Protein-lipin diet	1.11	0.64	0.95	330,000	0.7

ponents has been established as that of lipins for the platelets originating in the bone-marrow, and as that of globulins for the prothrombin and fibrinogen synthesized in the liver. Lipins and globulins are the source of the clotting substances of the blood, initially arising from the daily dietary. This nutritional basis for the clotting components of blood led us to a dietary treatment for certain hemorrhagic diseases. Studies were made of the relations between diet and the blood clotting factors in four dogs. The animals were maintained for forty-eight hours on a diet productive of bleeding, e. g., vegetables containing minimal amounts of protein, and fat and carbohydrates. Determinations made on the blood at the end of this period showed a decrease in the clotting factors and in the index. The dogs were then fed for forty-eight hours a diet productive of clotting, e. g., visceral proteins and unsaturated fats and oils, with the result that there was a definite rise over normal in the clotting factors and the index.

10. Widal, H.: Quart. J. M. Sc. **13**:257, 1920.

When the blood problems were studied among children, these were found to constitute two large groups: (1) those subject to bleeding, whose clotting substances were decreased in concentration, and (2) those subject to thrombosis, whose clotting substances were increased in concentration.

Bleeders found deficient in fibrinogen or prothrombin were maintained on an acid-forming diet high in globulins, a protein intake of about 5 Gm. per kilogram of body weight.

TABLE 8.—*Results with Diet to Increase the Clotting Function of the Blood*

Patient	Diagnosis	Date	Clotting Time	Bleeding Time	Prothrombin	Fibrinogen, %	Antithrombin	Platelets	Platelet Disintegration, %	Clotting Index
M.	Chronic appendicitis..	7/30	5'30"	1' 0"	1.0	0.28	1.07	460,000	48	0.3
		8/ 1	5'30"	1' 0"	0.93	0.37	1.0	240,000	44	0.3
		8/ 7	3'30"	1'30"	0.93	0.60	1.0	330,000	54	0.6
		8/ 9	3'30"	1'30"	0.87	0.54	1.0	225,000	42	0.5
A.	Hypertrophied tonsils	9/17	6'45"	.....	0.60	0.60	1.5	175,000	37	0.2
		10/16	5'45"	.....	0.93	0.64	1.07	150,000	37	0.5
		10/31	6'30"	.....	0.93	0.60	1.07	190,000	31	0.5
N.	Bleeder.....	3/10	6'15"	4'45"	0.39	0.75	1.4	175,000	37	0.2
		5/21	2'30"	1'30"	1.37	0.79	0.82	205,000	66	1.3
S.	Bleeder.....	8/30	4' 0"	2'30"	1.54	0.54	0.82	115,000	12	1.0
		9/17	4' 0"	2'30"	1.54	0.69	0.82	205,000	60	1.5
		10/ 8	4' 0"	2'30"	1.54	0.69	0.82	200,000	61	2.0

TABLE 9.—*Results with Diet to Decrease the Clotting Function of the Blood*

Patient	Diagnosis	Date	Clotting Time	Bleeding Time	Prothrombin	Fibrinogen, %	Antithrombin	Platelets	Platelet Disintegration, %	Clotting Index
W.	Partial nephrectomy for double pelvis of kidney	5/11	4'15"	1'30"	1.38	1.12	1.00	380,000	65	1.5
		5/14	4'30"	2' 0"	1.00	0.56	1.04	370,000	60	0.5
		5/21	3'15"	1'30"	1.54	0.69	1.04	420,000	60	1.1
F.	Cystic ovary, chronic appendicitis	7/26	3'30"	2' 0"	0.93	0.56	1.25	500,000	49	0.4
		8/ 2	3'15"	2' 0"	1.38	0.75	1.00	360,000	59	1.0
		8/ 4	4' 0"	2' 0"	1.38	1.03	0.75	350,000	65	1.8
		8/ 7	4' 0"	2' 0"	0.93	0.46	1.07	265,000	47	0.4
L.	Appendicitis.....	1/16	.....	.....	1.54	0.94	0.86	250,000	50	1.7
		1/25	.....	.....	1.00	0.94	1.00	200,000	40	0.9
R.	Inguinal hernia.....	8/11	.....	.....	1.38	0.60	0.83	250,000	60	1.0
		8/16	.....	.....	0.93	0.60	1.00	280,000	55	0.6
		8/20	.....	.....	1.00	0.54	1.00	240,000	46	0.5

Bleeders found deficient in platelets were maintained on an acid-forming diet high in unsaturated lipins, i. e., constituting two thirds of the caloric intake.

Patients the indexes of whose clotting functions were found to be high were maintained on a base-forming diet, consisting of 0.5 Gm. per kilogram of body weight, of fat as contained in the natural food without addition, and increased fluid intake.

Analyses of the diets to decrease clotting function and the diets to increase clotting function are given in tables 8 and 9.

Patient M. was admitted for operation and found to have a low clotting index (0.3) as the result of low fibrinogen. This patient was put on a diet to increase clotting, which doubled the blood fibrinogen and hence brought the clotting index to normal.

A. was advised to have a tonsillectomy, but a long-standing history of bleeding made A. an operational risk. The prothrombin was low (0.6), and the antithrombin high (1.5.). Diet brought the prothrombin and antithrombin to normal with a resultant normal clotting index.

N. was studied in the outpatient department because of purpuric spots and prolonged bleeding when bruised. N. showed a low level of prothrombin (0.39), a high level of antithrombin (1.4), and a low level of platelets. A diet to increase clotting readily brought the blood to a high normal clotting function.

S., a girl, aged 13, for four months since the onset of menstruation had had a persistent metrorrhagia. On a diet to increase clotting, the clotting index rose from 0.1 to 2 with a simultaneous cessation of the bleeding.

M., a boy, aged 9, had a typical thrombocytopenic purpura. The boy also had had a chronic eczema since the sixth month of life and was maintained on an approximately fat-free diet as part of the therapy for the eczema. With the onset

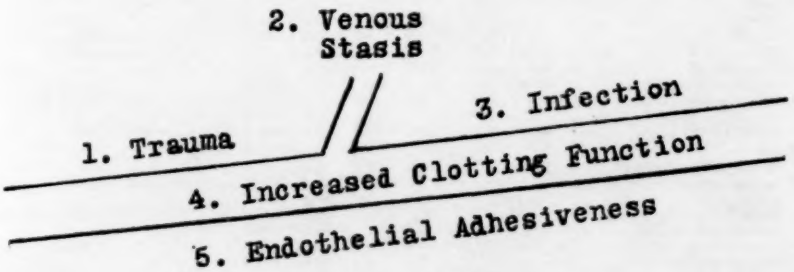


Fig. 4.—The conditions favoring thrombosis.

of purpura and with a decrease in the platelet count to less than 50,000, splenectomy was advised. A diet to increase clotting with two thirds of the calories in fat raised the platelet count to 340,000. At the time of writing, the boy had been free from purpura or eczema for two years.

DIETARY CONTROL OF THROMBOSIS AND EMBOLISM

Intravascular clotting produced by local trauma was first observed by Samuel.[11] Agglutination of platelets at the site of vascular damage was proved by Eberth (1886), and the liberation of prothrombin from traumatized tissue into the blood stream was demonstrated by Pickering.[12] Venous stasis was shown to be a contributory factor by Plass,[13] who characterized it as decreased plasma stability, increased erythrocyte sedimentation and increased fibrinogen content.

11. Samuel: Virchows Arch. f. klin. Chir. **51**:41, 1870.

12. Pickering, J. W.: The Blood Plasma in Health and Disease, London, The Macmillan Company, 1928.

13. Plass, E. O.: J. Lab. & Clin. Med. **12**:735, 1927.

TABLE 10.—*Diets to Increase the Clotting Function of the Blood*

1. Calories, 1,000: Protein, 8 Gm. per kilogram. Fat, two thirds of calories. Water, low. Acid, high. 20 per cent protein, 20 Gm.; 12 per cent carbohydrate, 33 Gm.; 68 per cent fat, 75 Gm.; water 435 cc.

Food	Measurements	Protein	Carbohydrate	Fat	Calcium	Acid	Base	Vitamin	Water
Breakfast:									
Stewed fruit (fresh)	4 tbsp.	0.2	3.8	0.2	18.3	....	2.01	ABC	18
Evaporated milk	2 tbsp.	3.8	4.5	3.7	66.8	....	0.7	ABCDEG	27
Egg	One	6.7	...	5.3	76.8	5.55	....	ABDEG	37
Bacon	2 strips	2.1	...	13.0	129.5	....	....	AB	4
Whole wheat bread	1 slice	0.9	5.2	0.1	25.9	0.3	....	AB	4
Dinner:									
Potato	4 tbsp.	1.0	8.4	...	38.5	....	2.8	ABC	30
Butter	2 pats	0.2	...	17.0	158.9	....	....	ABG	1
Liver	.....	19.0	...	5.3	123.9	....	....	.....	73
Milk	½ glass	3.3	5.0	4.0	71.2	....	1.81	ABCDEG	87
Supper:									
Brain	.....	8.8	...	9.3	118.9	....	....	.....	81
Spinach	Small serving	0.8	2.3	0.2	14.6	....	16.20	ABC	54
Egg yolk	One	3.1	...	6.7	75.0	5.33	....	ABD	1
Bone-marrow	.....	0.2	...	9.2	83.6	....			
Stewed fruit (fresh)	4 tbsp.	0.2	3.8	0.2	18.3	....	2.01	ABC	18
		13.1	6.1	25.6	310.4				435

2. Calories, 2,000: Protein, 5 Gm. per kilogram. Fat, two thirds of calories. Water, low. Acid reaction. 18 per cent protein, 90 Gm.; 16 per cent carbohydrate, 80 Gm.; 66 per cent fat, 148 Gm.; water, 817 cc.

Breakfast:									
Stewed fruit (dry)	4 tbsp.	0.9	20.7	0.4	90.0	...	2.01	ABC	18
Cooked cereal	6 tbsp.	2.5	10.0	1.1	59.9	1.9	....	ABE	1
Bacon	3 strips	3.2	...	19.4	174.6	?	....	AB	6
Liver	Serving	23.8	...	6.6	154.6	?	....	.....	91
Coffee									
Cream, 20 per cent	¼ cup	1.5	2.7	11.1	116.7	...	....	ABCE	44
Dinner::									
Peas	.....	3.6	9.8	0.2	55.4	...	1.3	ABCDE	85
Celery	.....	1.3	3.9	0.3	23.5	...	7.8	ABC	93
Butter	1 pat	...	...	8.5	76.5	...	...	ABG	1
Sweetbread	Serving	25.2	...	18.1	263.7	...	....	.....	105
Chicken fat	2 tbsp.	...	...	15.0	135.0				
Lettuce	.....	0.6	1.5	0.2	10.2	...	3.7	ABCDEG	47
Oil	.....	...	...	10.0	90.0				
Stewed fruit	½ cup	0.6	10.2	0.4	46.8	...	5.4	ABC	64
Supper:									
Whole wheat bread	1 slice	0.9	5.2	0.1	25.9	0.3	....	AB	3
String beans	.....	1.3	3.9	0.3	24.1	...	5.4	ABC	93
Butter	1½ pats	20.6	0.6	12.8	115.2				
Kidney	.....	20.6	...	2.9	110.9	?	....	ADG	94
Bone-marrow	.....	0.5	...	18.6	169.4				
Stewed fruit (fresh)	.....	0.6	10.2	0.4	48.0	...	3.0	ABC	64
Nut meats (Brazil)	.....	5.1	2.1	20.0	208.8	...	....	.....	1
		92.2	80.8	146.4	1999.2	...	....	.....	817

TABLE 11.—*Food Equivalents* for Increasing the Clotting Function of the Blood*

100 Gm. Portions	Protein, %	Fat, %
Meat:		
Beef, scraped	23.0	2.5
Brain	8.8	9.3
Caviar	30.0	7.6
Cheese (full cream)	25.9	33.7
Chicken (white meat)	17.6	7.6
Egg yolk	15.7	33.3
Fish (halibut)	18.6	5.2
Kidney	13.7	1.9
Liver (chicken)	22.4	4.2
Liver (veal)	19.0	5.3
Lungs	16.4	3.2
Sweetbread	16.8	12.1
Tongue	18.9	9.2
Fat:		
Bacon	10.5	64.8
Bone-marrow	2.2	98.8
Butter	1.0	85.0
Chicken fat	....	100.0
Cod liver oil	....	100.0
Goose fat		
Nut and nut products:		
Almonds	21.0	54.9
Brazil nuts	17.0	66.8
Peanuts	25.8	38.6
Peanut butter	29.3	17.1
Vegetable food:		
Beans, dry	22.5	1.8
Beans, green	4.7	3.8
Beans, lima, dry	18.0	1.5
Beans, lima, green	3.2	0.3
Lentils, dry	25.7	1.0
Peas, dry	24.6	1.0
Peas, green	7.0	0.5

* Dietary calculations were made by Miss Emma L. Samuel, research associate in nutrition, department of pediatrics.

Various attempts have been made to prevent thrombosis. Brooks [14] found that thrombi produced by artificial phlebitis were less extensive when the coagulabiliy of the blood was decreased by the oral adminis-

TABLE 12.—*Diets to Decrease the Clotting Function of the Blood*

1. Calories, 1,000: Protein, 0.25 Gm. per kilogram. Fat, only in natural foods. Basic reaction. Water, high. 7 per cent protein, 17 Gm.; 70 per cent carbohydrate, 173 Gm.; 23 per cent fat, 25 Gm.; water, 770 cc.

Food	Measurements	Protein	Carbohydrate	Fat	Calcium	Acid	Base	Vitamin	Water
Breakfast:									
Stewed fruit (fresh)	5 tbsp.	0.8	12.7	0.5	60.0	..	3.7	ABC	85
Cereal (cooked)	3 tbsp.	1.3	5.0	0.5	30.0	1	...	ABCE	7
Honey	1 tbsp.	0.1	24.4	...	100.0	..	...	AB	5
Milk	1 cup	7.9	12.0	9.6	170.8	..	4.3	ABCDEG	208
Dinner:									
Green vegetables									
Spinach	2 tbsp.	0.4	1.2	0.1	7.5	..	8.0	ABC	28
Cauliflower	2 tbsp.	0.4	1.2	0.1	7.5	..	1.6	AB	28
Tomatoes	1 small	0.4	1.2	0.1	7.5	..	1.4	ABC	24
Butter	¾ pat	0.1	...	6.4	58.8	..	...	ABDG	1
Potatoes	1 small	2.5	21.0	0.1	96.9	..	7.0	ABC	76
Stewed fruit (fresh)	5 tbsp.	0.8	12.7	...	60.0	..	3.7	ABC	85
Honey	1 tbsp.	0.1	24.4	...	100.0	..	...	AB	5
Supper:									
Green vegetables									
Asparagus	2 tbsp.	0.4	1.2	0.1	7.5	..	0.2	B	28
Carrots	2 tbsp.	0.6	2.7	0.1	14.5	..	3.2	ABC	26
Cabbage	2 tbsp.	0.4	1.2	0.1	7.5	..	1.8	ABC	27
Butter	¾ pat	0.1	...	6.4	58.8	..	...	ABDG	1
Rice	¼ cup	1.7	14.6	0.1	67.8	5	...	B	44
Fruit	5 tbsp.	0.8	12.7	6.4	60.0	..	3.7	ABC	85
Honey	1 tbsp.	0.1	24.4	...	100.0	+	...	AB	5

2. Calories, 2,000: Protein, 0.25 Gm. per kilogram. Fat, low. Basic reaction. Water, high. 5 per cent protein, 18 Gm.; 75 per cent carbohydrate, 360 Gm.; 20 per cent fat, 47 Gm.; Water, 1,176 cc.

Breakfast:									
Fresh fruit	Generous serv.	2.0	31.8	1.2	150.0	..	14.0	ABC	217
Honey	2 tbsp.	0.2	48.7	...	200.0	..	...	AB	11
Cereal	6 tbsp.	2.5	10.0	1.1	61.0	2	...	ABCE	14
Cream	2 tbsp.	0.8	1.4	5.5	60.3	..	...	ABCE	22
Coffee and sugar	2 tbsp.	...	25.0	...	100.0				
Dinner:									
Spinach	Serving	1.3	3.9	0.3	24.0	..	27.0	ABCG	92
Celery	Small serving	0.7	2.0	0.2	12.9	..	3.9	ABC	48
Potato	Small	1.9	15.7	0.1	73.1	..	5.25	ABC	59
Butter	2 pats	...	...	17.0	158.0	..	...	ABDG	2
Fruit	Generous serv.	2.0	31.8	1.2	150.0	..	14.0	ABC	217
Honey	2 tbsp.	0.2	48.7	...	200.0	..	....	AB	11
Tea and sugar	2 tbsp.	...	25.0	...	100.0				
Supper:									
Asparagus	Serving	1.3	3.9	0.3	24.0	..	8.0	B	94
Cauliflower	Serving	1.3	3.9	0.3	24.0	..	5.3	AB	92
Butter	2 pats	...	...	17.0	158.0	..	...	ABDG	2
Tomatoes, raw	Small serving	0.7	2.0	0.1	12.9	6	2.8	ABC	48
Lettuce, raw	Small serving	0.7	2.0	0.1	12.9	..	3.7	ABCDEG	48
Fruit	Generous serv.	2.0	31.8	1.2	150.0	..	14.0	ABC	200
Honey	2 tbsp.	0.2	48.7	...	200.0	..	...	AB	11
Tea and sugar	2 tbsp.	...	25.0	...	100.0				
		17.5	361.3	45.6	1971.0	2	90.8		1176

tration of citric acid. Rowntree [15] found that Howell's heparin prevented pulmonary thrombosis. But heparin is effective for two hours

14. Brooks, H.: J. Exper. Med. **10**:271, 1908.

15. Rowntree, L. G.: Experimental Thrombosis, J. A. M. A. **89**:58 (July 2) 1927.

with subsequent hypercoagulability. Pool [16] resorted to physical measures to improve the circulation and thus eliminate the stasis conducive to thrombosis. We have approached the problem from the dietary standpoint. It affords a continuous and cumulative effect in decreasing blood clotting function.[17]

Patient W. was admitted for removal of an extra lobe of the left kidney. Five days postoperatively, her clotting index was found to be high, and she was put on a diet to decrease clotting. In three days' time, the index went from 1.5 down to 0.5. She was then put back on a diet containing protein, and after a week her clotting index had risen to 1.1.

F. was operated on for cystic ovary and chronic appendicitis. The preoperative index was 0.4. Following the operation, the index rose to 1 and 1.8. After three days on a diet to decrease clotting, the clotting index dropped to 0.4 again.

SUMMARY

1. The methods of determination of the substances involved in coagulation of the blood are presented, i. e., prothrombin, fibrinogen, antithrombin, platelets, and the degree of platelet lysis.

2. The index of the clotting function of blood is a value calculated from the quantitative determinations of the clotting components.

3. A classification of diseases in which the clotting function of the blood is altered is given.

4. Pretonsillectomy studies of the clotting function are given for three groups of patients: (1) those with deficient clotting function; (2) those with normal clotting function who were previously suspected of being bleeders, and (3) those whose bleeding was due to dietary deficiency, who were treated by diet.

5. The dietary treatment of hemorrhagic diseases is presented. Analyses of diets for increasing clotting function and of diets for decreasing clotting function are given. Experiments on animals show that the tendencies to bleed or clot are definitely influenced by diet.

Case reports are presented, showing the results obtained with the diets to decrease and increase clotting, respectively.

This is a preliminary report. The studies are being continued.

16. Pool, E. H.: Systematic Exercises in Postoperative Treatment, J. A. M. A. **60**:1202 (April 19) 1913.

17. Kugelmass, I. N., and Tritsch, J. E.: Prenatal Prevention of Potential Hemorrhagic Disease of the New-Born, J. A. M. A. **92**:531 (Feb. 16) 1929.

INFLUENCE OF FEEDING ON CERTAIN ACIDS IN FECES OF INFANTS

III. A COMPARISON OF THE EFFECTS OF BREAST MILK AND OF WHOLE COW'S MILK ON THE EXCRETION OF VOLATILE ACIDS AND OF LACTIC ACID *

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AND

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CHICAGO

In previous communications,[1] we compared the volatile acid output of infants fed on breast milk with the output of those fed on diluted cow's milk plus lactose. It was found that the volatile acid output and the total titratable acidity were relatively constant when breast milk was employed and were extremely variable on the diluted cow's milk mixtures. Changing the diet had no great influence on the total quantity of acid excreted. A change from breast milk to cow's milk invariably caused the appearance of propionic acid in the stool. We showed that many factors other than diet influenced the number of stools and the excretion of acid.

The present study deals with the comparison of the acid output of infants on breast milk with that of infants on whole cow's milk.

As in our previous studies, this investigation embraces clinical considerations such as temperature, weight curve, number and weight of the stools, urinary observations and the influence of infection, in addition to the actual chemical determinations. The clinical observations will be reported in a later publication in which we shall discuss the relations of these chemical observations to the prevailing theories of infant nutrition.

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* Submitted for publication, Oct. 14, 1929.

* From the Department of Pediatrics of Michael Reese Hospital and the Northwestern University Medical School.

* From the Otto Baer Fund for Clinical Research, the Sarah Morris Hospital for Children and the Nelson Morris Institute for Medical Research of the Michael Reese Hospital.

1. Gerstley, J. R.; Wang, C. C.; Boyden, R. E., and Wood, A. A.: The Influence of Feeding on Certain Acids in the Feces of Infants: I. A Comparison of the Effects of Breast Milk and Modified Cow's Milk on the Excretion of Volatile Acids, Am. J. Dis. Child. **35**:580 (April) 1928; II. The Effect of an Excess of Lactose in Breast Milk and in Modified Cow's Milk, with Observations on a Parenteral Infection, ibid. **36**:289 (Aug.) 1928.

The chemical study includes the determinations of formic, acetic, propionic and lactic acid in the twenty-four hour specimens, as well as the total volatile acid, the total titratable acidity and the hydrogen ion concentration. The results are shown in tables 1, 2 and 3. For

TABLE 1.—*The Excretion of Acid and the Hydrogen Ion Concentration in the Feces of Breast Fed Infants*

			Total Cc. of Tenth-Normal Acid per 24 Hours				
Age	Infant	p_H	Formic	Acetic	Total Volatile	Total Titratable	Lactic
3	E	....	29.7	46.0	75.7	36.6	61.7
4	A	....	8.6	40.8	49.4		
4	F	....	17.2	40.1	57.3	....	44.8
4	D	....	76.1	23.9	100.0	39.4	84.5
5	A	....	26.6	29.4	55.4		
5	D	....	39.0	40.6	79.6	49.0	61.0
5	D	....	17.9	42.4	60.2	34.6	54.2
5	F	....	14.7	43.7	58.4	27.8	44.6
5	F	....	4.0	47.5	51.5	29.2	33.3
5	H	4.54	30.9	22.4	53.4	57.2	46.0
6	A	....	13.5	35.6	49.1		
6	A	....	26.5	25.0	51.5		
6	B	....	8.2	36.5	44.7	20.8	
6	D	....	42.3	38.1	80.4	87.5	62.1
6	D	....	46.2	19.4	65.6	40.0	50.3
6	E	....	7.6	27.4	35.0	12.1	21.7
6	E	....	13.2	37.2	50.4	21.5	28.5
6	F	....	32.5	41.6	74.1	43.1	58.1
7	D	....	22.7	14.4	37.1	17.2	58.7
7	D	....	32.2	19.4	51.6	33.9	62.8
7	G	4.71	12.6	36.7	49.3	49.3	39.5
7	G	....	21.5	63.8	85.3	88.7	58.1
8	G	4.70	....	84.6	84.6	87.8	45.9
8	G	4.58	17.3	56.5	73.8	86.0	46.9
10	A	....	56.9	11.7	68.6		
10	A	....	28.9	15.1	44.0		
10	B	....	6.8	61.4	68.2	21.2	
10	B	....	12.4	20.5	32.9	22.8	
10	F	....	22.0	82.0	104.0	59.2	59.3
10	F	....	17.4	50.4	67.7	38.2	42.5
11	A	....	19.5	14.7	34.2		
12	A	....	32.7	15.7	48.4		
13	M	4.64	17.0	25.8	42.8	51.3	33.8
13	M	4.36	22.8	47.9	70.6	121.8	43.3
13	A	....	26.6	24.0	50.6		
13	A	....	13.1	29.2	42.3		
14	B	....	33.2	73.3	106.5	84.6	
14	B	....	27.5	40.2	67.7	158.3	
15	B	....	42.1	84.3	126.4	72.5	
15	C	....	19.7	75.0	94.7	118.2	
15	C	....	12.5	32.3	44.8	29.6	
16	B	....	28.5	34.6	63.1	29.6	
16	B	....	11.9	11.5	23.4	10.0	
16	C	....	20.2	42.1	62.3	65.4	
16	C	....	19.0	26.0	45.0	47.5	
17	B	....	11.6	80.7	92.3	42.4	
17	B	....	17.5	55.5	73.0	38.4	
19	C	....	5.5	70.4	75.9	53.4	
20	C	....	26.6	33.3	59.9	43.9	

simplification, the experimental results on one child who showed reactions typical of all have been graphically represented in the accompanying chart.

EXPERIMENTAL DATA

With a few slight modifications which will be given presently, the same methods as described in a previous communication[2] were employed for the total

2. Gerstley; Wang; Boyden, and Wood (footnote 1, first reference).

titratable and volatile acids. After being weighed, the contents of each pail were rinsed into a graduated cylinder with distilled water and the volume of the total twenty-four hour specimen was made up to 500 or 1,000 cc., according to the size of the stool.

A well mixed sample of the aforementioned suspension was taken immediately for the p_H determination, type K Leeds and Northrup potentiometer with a platinum electrode and quinhydrone being used. The variation in the dilution of feces was found to have no influence on the p_H determination.

Another portion, about 100 cc., of the mixture was filtered, and the total titratable acidity was determined on portions of 25 cc. of the filtrate, hundredth-normal sodium hydroxide and phenolphthalein being used as indicators.

TABLE 2.—*The Excretion of Acid and the Hydrogen Ion Concentration in the Feces of Infants Fed on Whole Cow's Milk*

			Total Cc. of Tenth-Normal Acid per 24 Hours					
Age	Infant	p_H	Formic	Acetic	Propionic	Total Volatile	Total Titratable	Lactic
3	M	5.59	....	78.9	1.4	80.3	54.1	49.9
3	M	5.26	....	119.7	7.7	127.4	89.3	90.0
5	K	7.16	....	48.7	34.1	82.8	24.6	8.3
5	K	7.31	....	15.2	8.6	23.8	10.7	2.4
6	J	....	....	93.8	44.1	142.9	60.8	34.1
6	K	8.05	....	25.1	24.0	49.1	8.9	4.6
6	K	7.93	....	33.4	25.8	59.3	8.5	4.3
7	H	6.32	....	59.8	68.9	123.7	71.8	8.5
7	H	....	....	57.1	59.6	116.7	58.2	7.1
7	J	6.97	....	101.9	21.1	123.0	96.8	123.6
7	J	6.44	....	87.5	17.5	105.0	59.8	66.2
8	H	5.95	....	106.0	83.6	189.6	132.3	28.3
8	H	5.58	71.1	53.2	42.7	167.0	221.8	170.5
9	H	6.90	....	45.2	35.6	80.9	25.4	6.9
10	G	6.44	....	60.3	6.4	66.7	51.1	17.3
10	G	6.37	....	101.7	15.6	117.3	84.2	23.8
12	F	....	....	69.3	2.8	72.1	7.4	6.5

TABLE 3.—*The Hydrogen Ion Concentration in the Stools of Infants on Various Diets Arranged According to Age*

Breast Milk		Whole Cow's Milk				
4.54	4.58	5.59	7.31	6.97	5.95	6.44
4.71	4.64	5.26	8.05	6.44	5.58	6.37
4.70	4.36	7.16	7.93	6.32	6.90	
Averages 4.59		6.59				

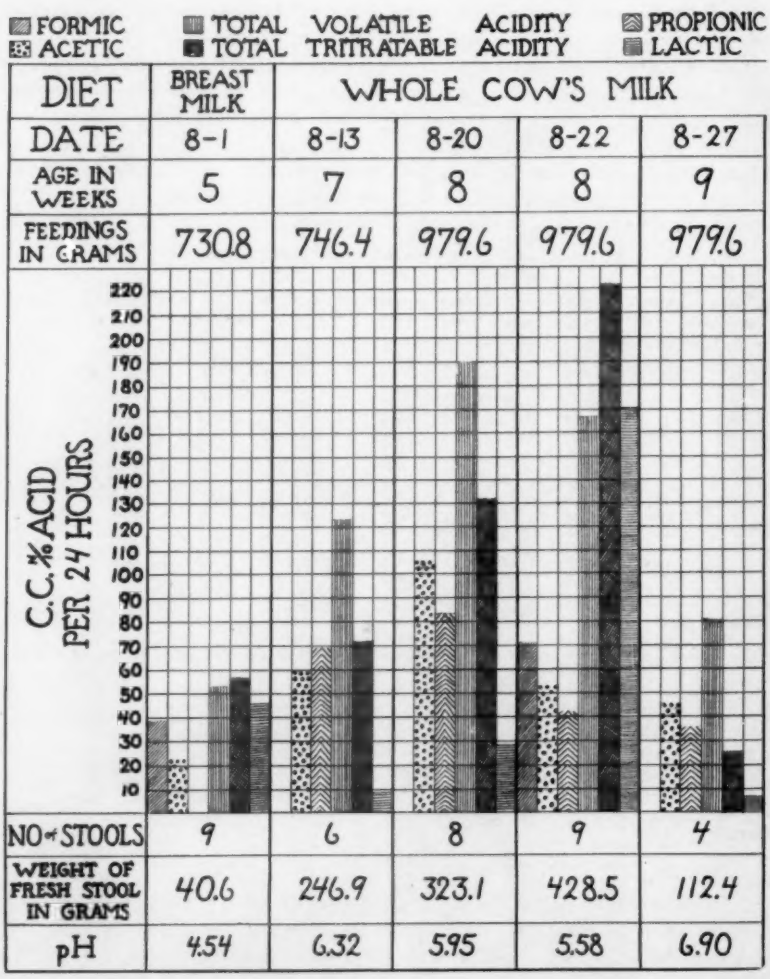
A third part, 300 cc. of the original suspension, was treated with 30 cc. each of 10 per cent sodium tungstate and two-thirds-normal sulphuric acid to precipitate any proteins present. Volatile acids were determined as before by the Duclaux method as modified by Gillespie and Walters,[3] 60 cc. of the filtrate, 25 cc. of tenth-normal phosphoric acid and distilled water to make up to 110 cc. being used.

For lactic acid the method described by Friedemann, Cotonio and Shaffer[4] was employed, with the following modifications: To 10 cc. of the protein-free

3. Gillespie, L. J., and Walters, E. H.: The Possibilities and Limitations of the Duclaux Method for the Estimation of Volatile Acids, J. Am. Chem. Soc. **30**:2027, 1917.

4. Friedemann, T. E.; Cotonio, M., and Shaffer, P. A.: The Determination of Lactic Acid, J. Biol. Chem. **73**:335, 1927.

filtrate 20 cc. each of 20 per cent copper sulphate and calcium hydroxide was added. After standing, with occasional shaking, for one-half hour or in the icebox over night, the mixture was filtered and portions of 10 cc. of the filtrate were used for the determination of lactic acid. All determinations were made in duplicate.



DIET	BREAST MILK	WHOLE COW'S MILK			
DATE	8-1	8-13	8-20	8-22	8-27
AGE IN WEEKS	5	7	8	8	9
FEEDINGS IN GRAMS	730.8	746.4	979.6	979.6	979.6
NO. STOOLS	9	6	8	9	4
WEIGHT OF FRESH STOOL IN GRAMS	40.6	246.9	323.1	428.5	112.4
pH	4.54	6.32	5.95	5.58	6.90

The influence of feedings of breast milk and whole cow's milk on the quantity of feces, the frequency of defecation, the excretion of volatile, total titratable and lactic acids, and the hydrogen ion concentration.

COMMENT

In contrasting the stools of infants fed on breast milk with those of infants fed on cow's milk, tables 1 and 2 demonstrate an intensification of the differences previously reported. The changes in the

volatile acids are apparent. On whole cow's milk, there is a decided tendency to an increase in the output of acetic acid and the development of propionic acid with the disappearance of formic acid. It is interesting to note that in spite of its low carbohydrate content, the total volatile acidity of the stool from infants fed on cow's milk is often decidedly higher than that of the stool from infants fed on breast milk. In contrast to the increase in volatile acids, the amount of lactic acid is decidedly less on cow's milk. This was true of all determinations except that under August 22, when the infant was suffering from severe diarrhea as shown by the decided increase in the weight of the stool. Calculation of these acids on the basis of per kilogram of body weight gives the same conclusions in a general way.

The results of the determinations of hydrogen ion concentration are given in table 3. Though the volatile acidity is often higher in infants fed on cow's milk than in those fed on breast milk and the acid obtained by titration may be about the same in the two mixtures, the hydrogen ion concentration of the stool of infants fed on cow's milk is always toward the alkaline side. Even when the volatile and titratable acids are astonishingly high, in the diarrheas of the dates August 20 and 22, and many times higher than in the infants fed on breast milk, the p_H never approaches the acidity of the stool of the infant fed breast milk. Whether this property is due to cow's milk itself or to the digestive secretions induced by cow's milk is a question for future study.

A glance at the chart as a whole gives some impressions that may have clinical significance. The stool of the breast-fed infant is small in weight and shows no great amount of volatile or titratable acid, but is decidedly acid in hydrogen ion concentration. The stools of an infant fed on whole cow's milk are extremely variable in weight and acidity, but with or without diarrhea the hydrogen ion concentration is much less than in the case of breast feeding. On cow's milk there always seems to be a certain relation between the amount of acid and the weight of the stool. One gets the impression that if the stools were all of the same weight the differences in acidity would not be great. Again, if one reduced the weight of the stool to that of the breast-fed infant, the acid output of the artificially fed infant would be even less than that of the breast-fed infant.

The chart suggests that the older clinicians were correct in their observations and incorrect in their interpretations. Unquestionably the diarrheal stools of infants fed on cow's milk contain more acid than those of the breast-fed infants, but the suggestion is that this increased acid does not come from any mysteriously increased fermentation. It seems merely an accompaniment of increased mass. The question thus becomes one of absorption.

There can be no question but that the amount of acid in the stool is independent of the amount of lactose in the food, for when the infants fed on cow's milk, with its 4 per cent lactose, have diarrhea, the acid excretion is much higher than in the diarrhea of infants fed on breast milk, with 7 per cent lactose. The absorption in the upper intestine seems to be the predominating influence.

CONCLUSIONS

When the diet of an infant on breast milk is changed to whole cow's milk, formic acid disappears from the stool, acetic acid predominates and propionic acid appears. While the total acid excretion is higher on whole cow's milk than on breast milk, the lactic acid diminishes. The total titratable acidity may be the same in the two stools, but the p_H of the stool of the infants fed on cow's milk is invariably toward the alkaline. As the acid output of infants fed on whole cow's milk with its 4 per cent lactose is often greater than that of infants fed on breast milk with its 7 per cent lactose, the acid output is obviously independent of the amount of lactose in the mixture. The older ideas of increased intestinal fermentation of lactose in cow's milk may not be as important as the problems of absorption of lactose.

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THE CARBOHYDRATE METABOLISM OF THE NORMAL NEW-BORN INFANT

II. THE EFFECT ON THE CONCENTRATION OF THE BLOOD SUGAR OF FEEDING VARIOUS SUGARS TO NEW-BORN INFANTS *

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In a previous paper we reported observations on the blood sugar values during fasting in normal new-born infants.[1] In this paper we report the results of studies on the dextrose, saccharose, lactose and dextrimaltose tolerance in new-born infants. In addition, the blood sugar curve after a breast feeding was determined in eighteen infants. We found a number of reports [2] in the literature on carbohydrate tolerance in infants ranging in age from 1 month to 2 years, but a careful search failed to reveal any studies on new-born infants.

TECHNIC

In all the work done, the values of the blood sugar were estimated on blood from the great toe, according to the technic described in a previous paper.[1]

Three hours after a feeding, the blood was taken and the sugar content was determined. Immediately after the blood was taken, 2 Gm. of dextrose, saccharose, lactose or dextrimaltose per kilogram of body weight was given in a 20 per cent solution. No difficulty was encountered in getting the infants to take the solution. If vomitting occurred, the infant was excluded from the study. Two grams of carbohydrate per kilogram of body weight was decided on: first, because Rumpf [3] found that the smallest amount of dextrose that produced an alimentary glycemia in older infants was 1.3 Gm. per kilogram of body weight, and second

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* From the Pediatric Service of the United Israel Zion Hospital.

1. Greenwald, H. M., and Pennell, S.: The Carbohydrate Metabolism of the Normal New-Born Infant: I. Average Concentration of the Blood Sugar in Normal New-Born Infants During Fasting, Am. J. Dis. Child. **39**:281 (Feb.) 1930.

2. Mogwitz: Monatschr. f. Kinderh. **12**:569, 1914. Bergmark: Jahrb. f. Kinderh. **80**:373, 1914. Nieman: Jahrb. f. Kinderh. **83**:1, 1916. Frank, A., and Melhorn, L.: Jahrb. f. Kinderh. **91**:313, 1920. Götzky: Ztschr. f. Kinderh. **9**:44, 1913. Bing and Winderlow: Ztschr. f. Kinderh. **9**: 64, 1913. Spence, J. C.: Quart. J. Med. **14**:314, 1921. Mertz, A., and Romimger, E.: Arch. f. Kinderh. **69**:81, 1921. Rumpf, F.: Jahrb. f. Kinderh. **105**:321, 1924. Brown, M. J.: Quart. J. Med. **18**:175, 1925. Tisdall, F. F.; Drake, T. Y. H., and Brown, A.: Carbohydrate Metabolism of Normal Infant, Am. J. Dis. Child. **30**:675 (Nov.) 1925. MacLean, A. B., and Sullivan, R. C.: Dextrose Tolerance in Infants and in Young Children, Am. J. Dis. Child. **37**:1146 (June) 1929.

3. Rumpf (footnote 2, ninth reference).

because this quantity closely approximates the amount of carbohydrate usually taken by a new-born infant under normal conditions after the secretion of milk in the mother has become established. For example, it has been fairly well established that an infant weighing from 6 to 7 pounds (2.7 to 3.2 Kg.) at the fifth or sixth day of life will take from 70 to 80 Gm. of breast milk per feeding, which contains approximately from 5 to 6 Gm. of lactose; this is about 2 Gm. of carbohydrate per kilogram of body weight.

Estimations were made of the blood sugar concentration during fasting and at one-half hour, one hour and two hours after the meal. Each sugar was administered to fifteen infants so that in all, sixty infants were studied. These infants ranged in age from 2 to 10 days.

RESULTS

Blood Sugar Values after Breast Feeding.—The blood sugar during fasting was determined and estimations were made one-half hour, one

TABLE 1.—*Increase in Blood Sugar Concentration After a Breast Feeding, During First Forty-Eight Hours of Life*

Infant No.	Age in Hrs.	Blood Sugar, Per Cent				
		Fasting	½ Hour	1 Hour	1½ Hours	2 Hours
1	2½	0.060	0.066	0.080	0.090	.....
2	9	0.074	0.083	0.074	0.074	0.069
3	14	0.074	0.073	0.074	0.069	0.071
4	16	0.062	0.071	0.071	0.064	0.066
5	16	0.069	0.066	0.067	.....	0.064
6	18	0.060	0.064	0.066	0.080	0.080
7	22	0.087	0.087	0.077	0.080	0.079
8	22	0.074	0.074	0.071	0.071	0.070
9	27	0.077	0.080	0.077	0.080	.....
10	30	0.087	0.080	0.083	0.077	.....
11	33	0.071	0.074	0.087	0.111	0.100
12	33	0.077	0.080	0.080	0.074	0.080
13	36	0.077	0.087	0.077	.....	0.077
14	40	0.069	0.083	0.091	0.087	0.083
15	40	0.062	0.062	0.062	.....	0.064
16	48	0.077	0.077	0.080	.....	0.105
17	50	0.087	0.082	0.076	0.077	0.087
18	52	0.082	0.064	0.063	0.066	0.069

hour, one and one-half hours and two hours after the breast feeding. In six infants the tolerance curve was followed from the first to the sixth day of life, estimations being made at the same time each morning.

In the eighteen infants studied after a breast feeding, no rise in the blood sugar concentration occurred after a breast feeding, during the first forty-eight hours of life, except in infants Nos. 11, 13 and 15 (table 1). This is undoubtedly due to the fact that the breasts secrete little or no milk, as a rule, during the first forty-eight hours after delivery. Colostrum, while it contains as much lactose as breast milk (6.8 to 7.59 per cent [4]), is secreted in but comparatively small amounts, and it is our opinion that not enough lactose is absorbed to produce a rise in the blood sugar curve during this period. Infants Nos. 11, 13 and 15 were born of multiparous mothers whose breasts secreted a fairly large

4. Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1923, vol. 1, p. 616.

amount of milk as early as the second day post partum. In the eighteen infants studied, a rise occurred in one and no rise in eight infants on the first day of life; on the second day there was an equal number in which no rise and a rise occurred. On the third day, six did and two did not show a rise in the blood sugar curve; on the fourth day, the breast feeding was followed by a rise in three infants and in two it was not (chart 1).

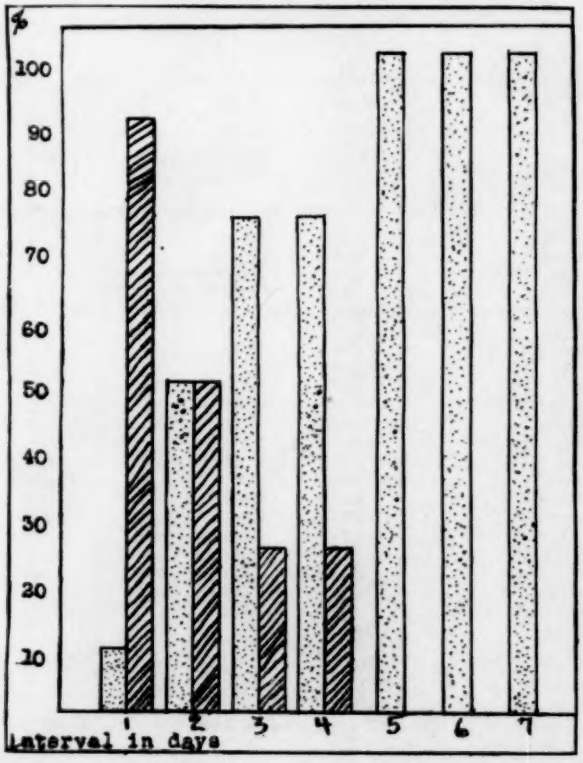

Chart 1.—Rise of blood sugar at intervals. The dotted columns indicate percentage of cases showing rise of blood sugar at various intervals; the lined columns, the percentage of cases showing no rise in blood sugar.

Table 2 is a summary of the blood sugar curves in the six breast-fed infants from the first to the sixth day of life. It will be seen that in only one infant a significant rise in the blood sugar concentration did not occur after a feeding until the fourth day of life (infant No. 4). In all the others, significant elevations occurred after the third day. In most instances the greatest value was usually reached one-half hour after the feeding. Exceptions were infants Nos. 12 and 16, in whom

the peak was not reached until two hours after a feeding. Whether this delayed rise was due to imperfect or tardy absorption in the gastro-intestinal tract or to changes in the carbohydrate metabolism is impossible to say at this time. The maximum value obtained was 0.182 per cent, one hour after a breast feeding, in infant No. 17.

The average values obtained during the first forty-eight hours of life are shown in chart 2. The average values obtained in the six infants studied from the third to the sixth day of life are shown in chart 3.

TABLE 2.—*Blood Sugar Concentration After a Breast Feeding in Infants Aged from 1 to 6 Days*

Infant	Age	Weight, Lbs. Oz.	Blood Sugar Per Cent				
			Starving	½ Hour	1 Hour	1½ Hours	2 Hours
1	16 hours....	7 10	0.069	0.066	0.077	.....	0.064
	40 hours....	7 3	0.062	0.062	0.062	.....	0.064
	3 days.....	7 5	0.069	0.111	0.095	.....	0.095
	4 days.....	7 7	0.080	0.111	0.095	.....	0.087
	5 days.....	7 10	0.066	0.118	0.111	.....	0.111
2	3 days.....	7 15	0.074	0.111	0.100	.....	0.100
	5 days.....	.....	0.083	0.154	0.182	.....	0.125
	6 days.....	.....	0.087	0.144	0.133	.....	0.083
3	3 days.....	7 6	0.077	0.077	0.095	.....	0.133
	5 days.....	.....	0.087	0.133	0.118	.....	0.095
	6 days.....	.....	0.074	0.118	0.105	.....	0.095
4	9 hours....	7	0.074	0.083	0.074	0.074	0.069
	33 hours....	.....	0.077	0.080	0.080	0.074	0.080
	57 hours....	.....	0.080	0.060	0.057	0.060	0.069
	81 hours....	.....	0.066	0.069	0.087	0.087	0.083
	105 hours....	.....	0.083	0.095	0.087	0.087	0.083
5	16 hours....	.....	0.062	0.071	0.071	0.064	0.066
	40 hours....	.....	0.069	0.083	0.091	0.087	0.083
	64 hours....	.....	0.069	0.071	0.074	0.087	0.091
	88 hours....	.....	0.069	0.080	0.087	0.111	0.091
	112 hours....	.....	0.066	0.074	0.083	0.105	0.100
6	2 days.....	.....	0.077	0.077	0.080	.....	0.105
	3 days.....	.....	0.091	0.111	0.118	0.100	0.100
	4 days.....	.....	0.091	0.125	0.118	0.095	0.091
	5 days.....	.....	0.071	0.133	0.100	0.071	0.077
	6 days.....	.....	0.095	0.166	0.154	0.105	0.077

Dextrose Tolerance.—Fifteen normal new-born infants, ranging in age from 2 to 10 days, were fed 2 Gm. of dextrose per kilogram of body weight, and the blood sugar curve was determined. In all but one a prompt and definite rise occurred in from one-half to one hour after the feeding. The highest point was 0.150 per cent in three cases. In twelve infants the blood sugar level during fasting was reached at the end of two hours. In the remaining three infants there was a decided lag. In one, the blood sugar reached a higher level two hours after the ingestion of dextrose than it did one hour after ingestion. In two infants the blood sugar was exactly the same at the end of two hours as after one hour. Maximum absorption occurred at the end of one-half hour in seven infants and at the end of one hour in an

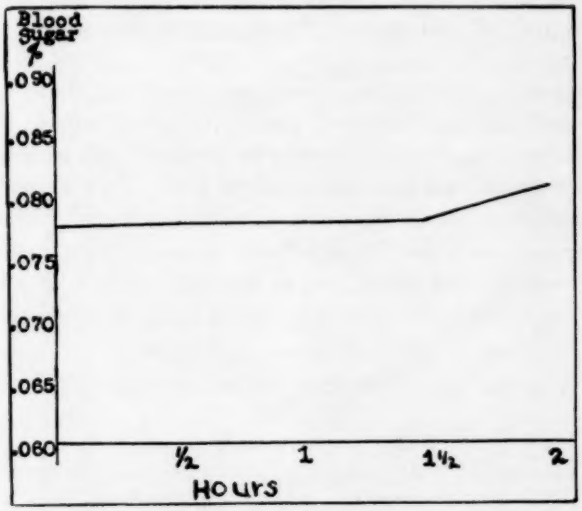

Chart 2.—Curve following breast feeding during first forty-eight hours of life.

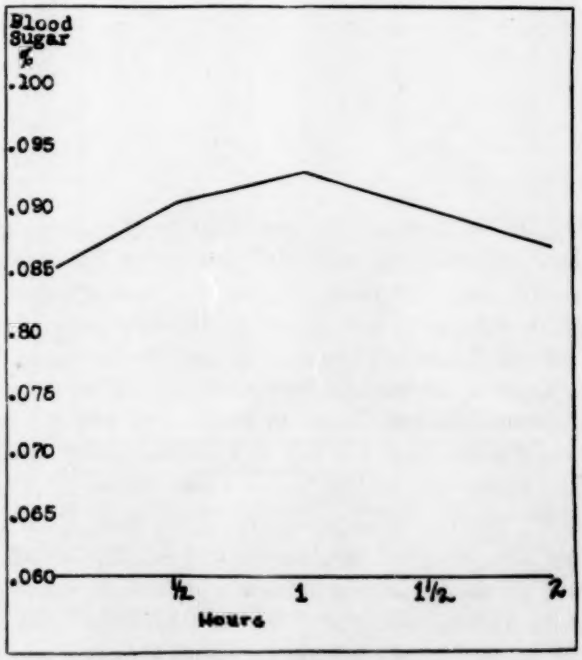

Chart 3.—Curve following breast feeding from the third to the sixth day of life.

equal number. The average value at the end of one-half hour was 112 mg.; at the end of one hour, 115 mg., and at the end of two hours, 90 mg. (table 3).

These blood sugar curves correspond closely to those obtained by MacLean and Sullivan [5] in their studies on the dextrose tolerance in infants varying in age from 5 weeks to 3 years. A comparison of the alimentary dextrose tolerance of children from 5 weeks to 3 years of age and new-born infants with that of adults is given in chart 4. The sugar tolerance curve in the new-born infant is essentially the same as in older infants and adults, except that the curve is at a lower level.

Cane Sugar Tolerance.—In only two infants were maximum values of 140 mg. or above obtained after the ingestion of cane sugar, as compared with the values obtained in three infants after the ingestion

TABLE 3.—*Dextrose Tolerance*

Infant	Age in Days	Weight	Blood Sugar Per Cent			
			Starving	½ Hour	1 Hour	2 Hours
1	7	7:4	0.069	0.111	0.133	0.157
2	7	7:5	0.077	0.080	0.091	0.091
3	6	6:15	0.080	0.111	0.125	0.125
4	7	8:0	0.062	0.091	0.133	0.154
5	6	8:8	0.069	0.144	0.144	0.083
6	6	7:10	0.083	0.125	0.144	0.105
7	5	8:6	0.062	0.118	0.154	0.069
8	5	7:13	0.062	0.111	0.095	0.095
9	4	7:13	0.069	0.100	0.125	0.105
10	9	6:2	0.077	0.154	0.118	0.100
11	9	7:10	0.074	0.111	0.091	0.077
12	5	7:13	0.087	0.100	0.118	0.077
12	8	7:13	0.071	0.111	0.080	0.086
14	5	5:12	0.071	0.111	0.091	0.069
15	4	6:7	0.069	0.095	0.083	0.077

of dextrose. In two infants the two hour level was higher than the one hour level, as compared with that obtained in one infant following the dextrose feeding. In eleven infants, the fasting blood sugar level was reached at the end of two hours; in the remaining two, the curve showed a definite downward trend at the end of this period. Maximum absorption occurred at the end of one-half hour in six infants, and at the end of one hour in seven infants. The average value at the end of one-half hour was 0.105 per cent; at the end of one hour, 0.112 per cent, and at the end of two hours, 0.080 per cent. The two hour value with cane sugar feeding was closer to the blood sugar level during fasting than that obtained after feeding any other sugar (table 4).

Lactose Tolerance.—In two infants a maximum value of 140 mg. was obtained. In only one infant was the two hour value higher than the one hour value. In two infants the two hour value was the same as

5. MacLean and Sullivan (footnote 2, twelfth reference).

the one hour value. The other curves were at a distinctly lower level than the curves obtained following the ingestion of dextrose or saccharose. In one, practically no rise occurred. The maximum value was obtained at the end of one-half hour in five infants and at the end

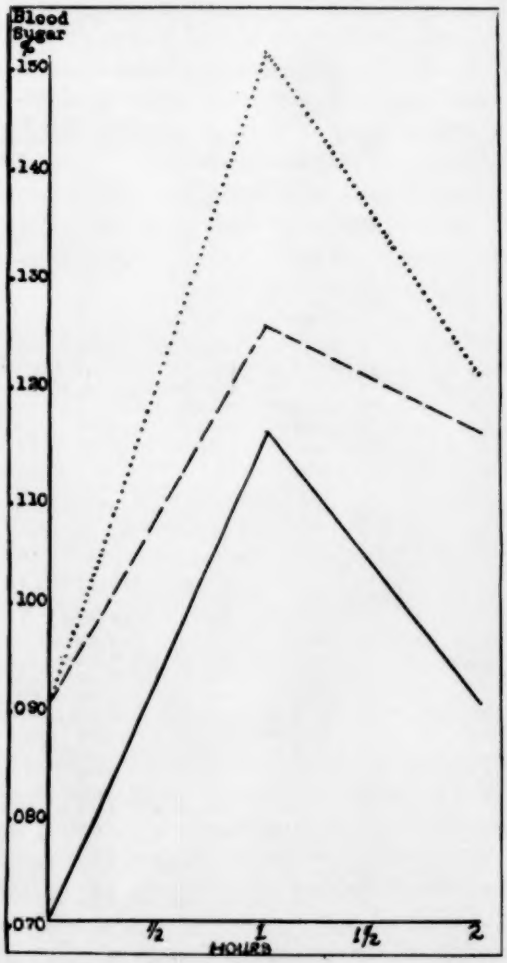

Chart 4.—Curves of blood sugar concentration of adults, infants aged from 5 weeks to 3 years and new-born infants, after the ingestion of dextrose. The dotted line indicates blood sugar concentration of adults; the dash line, the concentration of infants from 5 weeks to 3 years of age (MacLean and Sullivan), and the solid line, the concentration of new-born infants.

of one hour in nine. In nine infants the blood sugar level during fasting was reached at the end of two hours; in the remaining six, there was a definite lag. The average value at the end of one-half hour was 0.1

per cent; at the end of one hour, 0.114 per cent, and at the end of two hours, 0.09 per cent. Apparently, there is a slower rate of absorption for lactose than for dextrose or cane sugar (table 5).

Dextrimaltose Tolerance.—The most irregular curves were obtained following the feeding of dextrimaltose. In four infants practically flat curves were obtained. In one infant, no rise occurred. In three infants

TABLE 4.—*Cane Sugar Tolerance*

Infant	Age in Days	Weight	Blood Sugar Per Cent			
			Starving	½ Hour	1 Hour	2 Hours
1	6	7:1	0.060	0.100	0.111	0.091
2	4	6:1	0.064	0.083	0.091	0.111
3	10	7:6	0.071	0.111	0.118	0.077
4	4	5:1	0.069	0.133	0.125	0.069
5	4	7:0	0.066	0.133	0.154	0.071
6	3	6:15	0.069	0.125	0.133	0.074
7	7	6:12	0.066	0.111	0.111	0.066
8	7	6:6	0.064	0.087	0.111	0.087
9	7	7:2	0.052	0.071	0.080	0.080
10	5	8:1	0.071	0.074	0.133	0.095
11	8	7:14	0.077	0.125	0.100	0.077
12	3	...	0.059	0.125	0.111	0.077
13	2	7:8	0.077	0.111	0.166	0.083
14	5	9:0	0.059	0.118	0.057	0.053
15	3	7:5	0.071	0.091	0.100	0.080

TABLE 5.—*Lactose Tolerance*

Infant	Age in Days	Weight	Blood Sugar Per Cent			
			Starving	½ Hour	1 Hour	2 Hours
1	3	7:4	0.055	0.100	0.105	0.071
2	5	6:2	0.080	0.111	0.111	0.091
3	6	6:14	0.077	0.118	0.105	0.105
4	5	6:12	0.080	0.091	0.105	0.069
5	4	6:11	0.087	0.118	0.095	0.071
6	4	7:8	0.077	0.105	0.125	0.105
7	3	5:5	0.057	0.091	0.080	0.069
8	2	6:0	0.077	0.144	0.111	0.080
9	2	5:10	0.071	0.095	0.144	0.133
10	10	6:4	0.074	0.105	0.125	0.080
11	2	6:13	0.062	0.062	0.100	0.087
12	6	8:1	0.083	0.095	0.118	0.133
13	8	7:5	0.074	0.087	0.091	0.091
14	4	6:13	0.077	0.095	0.105	0.077
15	4	7:10	0.080	0.125	0.166	0.100

a high value of 0.14 per cent was found. The maximum rise occurred at the end of one-half hour in only three infants. In four infants the maximum rise occurred at the end of one hour; in five infants the two hour value was higher than the one-half hour or one hour value; in three infants the blood sugar level during fasting was reached at the end of two hours, and in three infants, although the curve showed a downward trend, the two hour value was still definitely above the blood sugar concentration during fasting. In other words, eight infants

showed a definite lag with dextrimaltose, whereas only six showed it with lactose; only two with cane sugar and three with dextrose. The average value at the end of one-half hour was 0.095 per cent; at the end of one hour, 0.102 per cent, and at the end of two hours, 0.095 per cent (table 6).

The dextrimaltose curve closely parallels that for the breast-fed infants and is much flatter than the curve found in infants fed with other sugars. The amount of breast milk taken by each infant was not controlled, and it is therefore obviously incorrect to compare the curves obtained after a breast feeding with the curves obtained after feeding definite amounts of various sugars. If it is assumed that the breast-fed infants studied received adequate amounts of milk, it must be concluded that the best tolerance is for lactose, as it exists in breast milk. It is unlikely that the flatness of the curve is

TABLE 6.—*Dextrimaltose Tolerance*

Infant	Age in Days	Weight	Blood Sugar Per Cent			
			Starving	½ Hour	1 Hour	2 Hours
1	10	6:12	0.074	0.100	0.105	0.095
2	10	8:0	0.080	0.105	0.118	0.105
3	?	7:0	0.080	0.095	0.087	0.095
4	7	6:9	0.066	0.077	0.125	0.154
5	7	7:7	0.064	0.095	0.111	0.083
6	4	6:0	0.071	0.125	0.154	0.118
7	4	6:13	0.069	0.105	0.133	0.125
8	7	5:15	0.062	0.082	0.157	0.060
9	8	7:0	0.077	0.111	0.144	0.111
10	6	7:2	0.060	0.062	0.052	0.059
11	5	7:2	0.069	0.118	0.111	0.066
12	4	7:15	0.071	0.091	0.100	0.105
13	4	8:8	0.077	0.091	0.087	0.095
14	2	7:8	0.071	0.087	0.071	0.069
15	1	7:2	0.066	0.083	0.080	0.091

due to delayed absorption since it is generally conceded that breast milk is the ideal food, particularly for the new-born infant. In addition, the presence of protein, fat and salts in breast milk may be a factor in the absorption and assimilation of lactose. This phase of the problem is being studied at the present time, and the results will be reported in a subsequent paper.

It is questionable whether the flatness of the curve following the ingestion of dextrimaltose may be considered due to an increased tolerance for this sugar, as was the case with lactose present in breast milk. It is more likely that dextrimaltose is absorbed more slowly than the other sugars, since with no other sugar did we obtain as large a number of flat and lag curves.

Chart 5 gives the average values for cane sugar, dextrimaltose, lactose and saccharose. With all sugars, the maximum value was obtained at the end of one hour. The curves obtained following the

feeding of lactose, cane sugar and dextrose closely parallel each other, except that the two hour period for cane sugar more closely approximated the blood sugar level during fasting. The average curve for dextrimaltose showed a decided lag. The best absorption occurred with dextrose. The curve obtained after feeding dextrose closely approximated the curves obtained in adults and older children after the ingestion of dextrose, except that it was at a definitely lower level, as is indicated by chart 4.

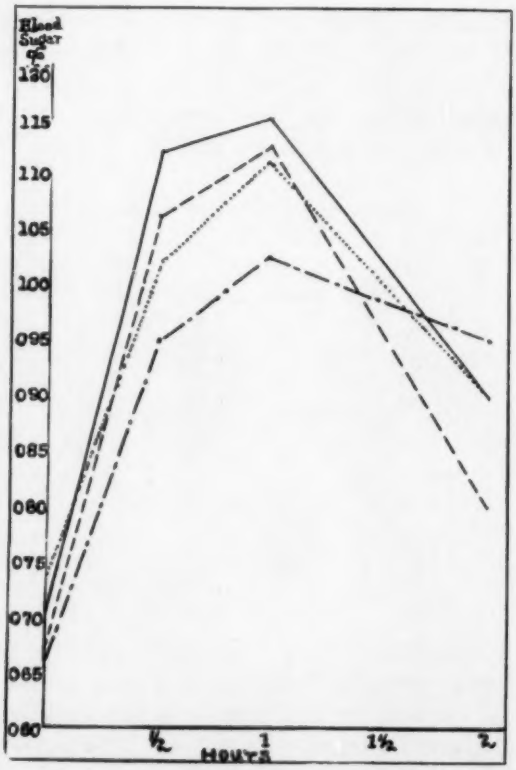

Chart 5.—Average curves for dextrose, saccharose, lactose and dextrimaltose. The solid line indicates course of dextrose; the dash line, saccharose; the dotted line, lactose, and the dot and dash line, dextrimaltose.

SUMMARY

In eighteen infants the blood sugar concentration was followed after a breast feeding during the first forty-eight hours of life; practically no increase in the blood sugar concentration occurred. This was most likely due to an insufficient secretion of breast milk during this period. In seven infants, the blood sugar curve after a breast feeding was studied from the first to the sixth day of life. A definite rise in the blood sugar concentration occurred in from one-half to one hour in practically all

infants after the second day of life. From the curves obtained, it is concluded that the best tolerance is for lactose as it occurs in breast milk.

Sixty infants were fed definite amounts of dextrose, lactose, saccharose and dextrimaltose; each sugar was administered to fifteen infants. The blood sugar curve after a dextrose meal is at a definitely lower level during the neonatal period than at any other period in life. The best rate of absorption occurred after the ingestion of dextrose, saccharose, lactose and dextrimaltose in the order in which they are named. The most irregular curves were obtained with dextrimaltose; with dextrose, saccharose and lactose fairly uniform curves were obtained.

THE COMPARATIVE VALUE OF TOXOID AND OTHER AGENTS IN THE IMMUNIZATION OF THE PRE-SCHOOL CHILD AGAINST DIPHTHERIA*

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The incidence and mortality of diphtheria have been effectively reduced by the extended introduction of immunization against the disease. In the popularization of such a procedure, the fine work of Park and his associates deserves a place as a distinctly outstanding achievement for public health. The procedure has been adopted in the public schools of hundreds of communities. Through these agencies tangible statistical evidence of its benefits has been recorded. The complete effectiveness of the immunization program has been lessened by the difficulty of reaching the preschool child, among which group the highest incidence of diphtheria prevails, and by the imperfections of methods and materials used.

To eradicate diphtheria completely, immunization must become as routine a medical practice for the preschool child as is the administration of orange juice a dietetic measure for the infant. Such custom, however, must be made secure by perfecting methods and materials now available.

Errors due to improper performance of the Schick test, because of poor technic, materials or interpretations, and those due to variable potency of immunizing material must be eliminated if one is to establish diphtheria immunization as a universal practice.

Private physicians and public agencies in this country have practically confined their work in diphtheria immunization to the use of toxin-antitoxin. This material, however, has two distinct disadvantages. The first is its variable protective value—about 25 per cent of the patients remaining insufficiently immunized after three doses of toxin-antitoxin; the second is the danger of serum sensitization following its use.

THE PROTECTIVE VALUE OF TOXIN-ANTITOXIN AS NOW ADMINISTERED

The results obtained in the public schools of Milwaukee after three doses of toxin-antitoxin, for the years 1925 to 1928, are given in table 1. These results, showing a low percentage of immune patients, obtained

* Submitted for publication, Oct. 31, 1929.

under the careful supervision of the epidemiologist, Dr. M. R. French, are, we believe, representative of results obtained among school groups generally in this country.

An equally low percentage of immune patients was reported from the Gary, Ind., schools,[1] in which, of 1,668 retested persons who had received toxin-antitoxin from four different biologic manufacturers, 1,170 showed a negative reaction to the Schick test, 30 per cent of the patients remaining susceptible to diphtheria.

In Whitefish Bay, a suburb of Milwaukee, the size and organization of the village made it possible for one physician, the health officer, to make all the injections and tests himself, thus obviating the possible variability of individual differences of technic. Of 392 children receiving three injections of toxin-antitoxin there, 33.7 per cent remained susceptible to diphtheria.[2]

During the five year period from 1922 to 1927, of the children receiving toxin-antitoxin in our office, 361 returned for a Schick test. Of these, 283 were recorded as having negative reactions, 78 per cent

TABLE 1.—*Immunization Results in Milwaukee Public Schools After Three Doses of Toxin-Antitoxin*

Year	Number of Positive Reactions	Number of Negative Reactions	Per Cent Immune
1925	489	1,875	85
1926	4,626	6,867	62
1927	2,133	6,741	75
1928	146	325	69

exhibiting immunity. This figure represents results obtained with various kinds of toxin-antitoxin, including some from the New York State Board of Health. Schick tests on this series were done with test outfits obtained in the market. Many of the earlier tests were done without controls, and therefore the result obtained, namely, 78 per cent immune patients, may be regarded as an unusually liberal estimate of the value of toxin-antitoxin as generally used in private practice.

Fifteen children who showed a positive reaction to the Schick test were given a second series of injections of toxin-antitoxin. Children given such injections were always desensitized in the usual manner before the toxin-antitoxin was administered. Of the group of fifteen patients, one child received only a single dose, which precipitated a pronounced urticaria within one-half hour following the injection. No further injections were given to this child. Of the other fourteen children, twelve became immune after three injections of the second series,

1. Smythe, M. G., and Nesbit, O. B.: Diphtheria Prevention Work, J. Indiana S. M. A. **21**:155, 1928.

2. Personal communication from Dr. Edwin B. Gute, Health Officer Whitefish Bay, Wisconsin.

while two continued to show positive reactions to the Schick tests. Although only two children continued to give positive reactions to the Schick test, the result is noteworthy because single instances of inadequate protection do more to discount the value of the method in the public mind than any number of successful immunizations. Besides this unfortunate effect on the public attitude, it becomes increasingly difficult to have children brought back for additional injections.

During the winter of 1927, a number of children were given three injections of New York State Board of Health toxin-antitoxin that had been purchased in New York City. On account of the inadvertent omission on our charts of sources of material used at that time, many of this series are included among the general group of toxin-antitoxin from various commercial houses. The use of the New York State Board of Health material is probably an additional reason why the total percentage of immune patients obtained with toxin-antitoxin in our office is higher than that reported by others. Our records showed the use of such material in ten children. Of these patients, eight became immune, and two continued to give positive reactions. Five other children who had had a positive reaction after three injections of a commercial toxin-antitoxin, were given a second series of three injections with New York State Board of Health material. All five patients then showed a negative reaction to the Schick test. Though this group of patients is a small one, it does seem to indicate that a higher percentage of immune patients is obtained after the use of New York State Board of Health toxin-antitoxin than after the ordinary commercial products of toxin-antitoxin.

Conversations with many pediatricians confirm the opinion that these observations are not unique. Moreover, they do not take into consideration the unfortunate, though unusual, circumstance, due to variable potency of material, that supposedly immune persons contract diphtheria. Rhoads' experience at the Cook County Hospital in 1926 is an example of such an occurrence.[3] During an epidemic of diphtheria at the Cook County Hospital in 1926, it was found that 67.2 per cent of the nurses who had previously had toxin-antitoxin, and had been regarded as immune, gave a positive reaction to the Schick test. Only 58.3 per cent of the nurses who had not had any toxin-antitoxin gave a positive reaction to the Schick test. Furthermore, of twenty-nine cases of diphtheria among the nurses, nine had had toxin-antitoxin. Such unfortunate incidents may obviously have to do with improperly performed Schick tests or with what is equally dangerous, assumption that immunity is present and omission of a Schick test. The influence of

3. Rhoads, Paul S.: Commercial Preparations of Diphtheria Toxin-Antitoxin. Protecting Value in the Nurses of Cook County Hospital, J. A. M. A. **90**:254 (Jan. 28) 1928.

variations in the diphtheria toxin content of Schick outfits on the accuracy of the Schick test was long ago emphasized by Zingher.[4] An account of other possible errors in the performance of the Schick test is given in a masterly exposition of the subject by Dudley.[5]

THE FACTOR OF SERUM SENSITIZATION WITH TOXIN-ANTITOXIN

In hundreds of thousands of injections of toxin-antitoxin, no serious accident has occurred according to Park.[6] Though the danger of serum sensitization following toxin-antitoxin may be slight, the fear of its occurrence is commonly prevalent. Gordon and Creswell [7] showed that, of persons immunized to toxin-antitoxin, 74.1 per cent had a serum reaction following a subsequent therapeutic serum. Of those not so sensitized, 18 per cent would react naturally. Even those who minimize the importance of this objection to toxin-antitoxin attempt to desensitize those subjects who have received toxin-antitoxin before administering therapeutic serums. To obviate the possibility of serum sensitization, the use of toxin-antitoxin prepared from some other serum than that of the horse has been urged. Sheep serum toxin-antitoxin has been widely employed for this purpose.

THE USE OF SHEEP SERUM TOXIN-ANTITOXIN

One hundred and four children were given three doses of sheep serum toxin-antitoxin purchased in the market. One hundred and one of these children returned for a Schick test about six months later. Of them, seventy-one were immune, and thirty showed a positive reaction to the Schick test. Schick tests on this group were done with material prepared by the New York State Board of Health Laboratories. The tests were always done by the same person (F. R. J.), a control test being made on the opposite arm. The tests were read by one of us on the fifth day. All degrees of positiveness, faint or otherwise, were recorded as positive reactions. It was our impression that Schick tests done with the New York State Board of Health material gave more clearcut readings than those done with material purchased in the open market, prepared by commercial laboratories.

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4. Zingher, Abraham: Accuracy of the Schick Reaction. Influence of Variations in Diphtheria Toxin Content in Schick Outfits, J. A. M. A. **75**:1333 (Nov. 3) 1920.

5. Dudley, Sheldon F.: Schick's Test and Its Applications: Critical Review, Quart. J. Med. **22**:321, 1929.

6. Park, William H., and Schroeder, May: Practical Points About Active Immunization Against Diphtheria and Scarlet Fever, Am. J. Pub. Health **18**:1455, 1928.

7. Gordon, J. E., and Creswell, S. M.: To What Extent do Toxin-Antitoxin Mixtures Sensitize to Therapeutic Serum? J. Prevent. Med. **3**:21, 1929.

It is interesting to record that nine of these thirty children showing a positive reaction to the Schick test showed a negative reaction on retests at intervals of seven weeks to four months later. Such an occurrence may be explained by the concept of primary and secondary stimuli taught us by Glenny and his co-workers and discussed by Dudley [5]:

> Glenny and Sudmersen (1921) and Glenny and Allen (1922) published work which showed that when a dose of diphtheria toxin-antitoxin mixture is given to an animal, which has never been inoculated before, and which has no diphtheria antitoxin in its blood, there is a latent period of about three weeks before any antitoxin can be detected in the animal's blood. Antitoxin then appears, and its quantity gradually increases to reach a maximum about eight weeks after inoculation. The antitoxin titre then slowly declines. This is the type of response to a primary antigenic stimulus in an animal with no previous experience of the antigen employed. If, after all, or nearly all, the antitoxin has disappeared from the blood of an animal which has had such a primary stimulus, a second injection of toxin-antitoxin mixture is given, antitoxin reappears in three days instead of three weeks, and the antitoxin titre reaches its maximum in about eight days instead of weeks. Moreover, the quantity of antitoxin produced is ten to one hundred times the amount produced by the original primary stimulus. An antigenic inoculation which produces this type of response is termed a secondary stimulus. Thus, in an organism that has been sensitized by an antigen, although no antibody may be present in the blood, yet the animal as regards its immunity, is in quite a different state to one which is not sensitized. Such a sensitized, or experienced, animal may respond to further antigenic inoculations, or secondary stimuli, even if of much smaller intensity than the primary stimulus, by making antibody at ten times the rate and ten times as potent as an inexperienced animal. . . . O'Brien has shown that even the minute dose of diphtheria toxin contained in the Schick injection is often sufficient to induce a rise in the antitoxin titre of the blood from below to above Schick level (0.03 units per cc.).

THE USE OF LARSON'S RICINOLEATED TOXIN

Ten children who continued to show a positive reaction to the Schick test after three doses of commercially obtained horse serum toxin-antitoxin were given one dose of Larson's ricinoleated toxin. The youngest child in the group was 3½ years old. Of these ten children, six became immune, and the Schick test of four remained positive. These four children were all 5 or 6 years of age.

THE USE OF TOXOID AS AN IMMUNIZING AGENT AGAINST DIPHTHERIA

Ramon [8] recently published the results of his experiences with diphtheria anatoxin (toxoid). Such a preparation, made by detoxifying diphtheria toxin with formaldehyde, is stable and nontoxic.

8. Ramon, G., and Helie, G. Illingworth: Diphtheria Prophylaxis in France: Experiments with Anatoxin Vaccination, J. A. M. A. **91**:1028 (Oct. 6) 1928.

Containing no foreign serum, it cannot produce sensitization to subsequent serum injections.

In the United States, despite Zingher's [9] demonstration of toxoid superiority to toxin-antitoxin, the latter remains the prevailing method for diphtheria immunization.

Fitzgerald [10] and Moloney [11] of the Connaught Laboratories, University of Toronto, have made significant contributions to the use of toxoid. They perfected the method of its preparation, providing a uniform material possessing a high antigenic value. This product has been widely and effectively used in Canada.

The Connaught Laboratory furnished us with a supply of their toxoid for a limited clinical test. With this material, a group of unselected children in private practice were immunized. The technic employed was that advised by Dr. Moloney of the Connaught Laboratories, the use of three doses containing 0.5, 0.5 and 1 cc. respectively. The doses were given at intervals of three weeks. In some instances, Ramon's dosage was followed. In a small number of subjects the reaction test was performed, but when it was learned from Dr. Moloney that in the preschool child reactions were almost negligible, this test was dispensed with, the parent being warned that in a small percentage of cases a slight reaction might be expected.

Ninety-three children who had never had any previous injections of toxin-antitoxin were given three doses of Connaught Laboratory diphtheria toxoid. Of them, sixty-five were below 2 years of age, twenty-five between 2 and 6 years and three children were over 6 years of age. After three doses of toxoid, ninety-two subjects showed a negative reaction to the Schick test; one child below 2 years of age exhibited a slightly positive reaction on the fifth day of reading, which was not discernible on the following day. Accepting the fifth day reading, which was the practice with the others of this group, and counting this instance positive, 98 per cent of the group were immunized —the identical results obtained by Zingher with a preparation of Ramon's anatoxin.

Thirty-five children, who had exhibited a positive reaction from the Schick test after other material, were given three doses of toxoid in the outlined manner. Thirty-four of the children gave negative reac-

9. Zingher, Abraham: Immunity Results with Diphtheria Toxoid (Modified Toxin-Antitoxin) and 1/10 L + Mixtures of Toxin-Antitoxin, Proc. Soc. Exper. Biol. & Med. **22**:462, 1924-1925.

10. Fitzgerald, J. G.: Diphtheria Toxoid as an Immunizing Agent, Ann. Clin. Med. **5**:870, 1927. Moloney, P. J.: The Preparation and Testing of Diphtheria Toxoid (Anatoxine-Ramon), Am. J. Pub. Health **16**:1208, 1926.

11. Moloney, P. J., and Fraser, C. J.: Préparation de l'anatoxine diphtérique et vérification de ses propriétés, Ann. de l'inst. Pasteur, **42**:1420, 1928.

tions to the Schick test; one child, a 13 year old girl, continued to give a positive reaction.

TECHNIC OF THE SCHICK TEST

Since we recognized the importance of proper performance of the Schick test in a study of this sort, all tests were done by one person (F. R. J.), and they were always done at the office. The materials were mixed and used on the same afternoon. Vim Schick syringes and needles were employed. Material for both the test and control was a New York State Board of Health product, purchased in New York City. This was kept in a refrigerator in the office.

Dudley [5] thought that the most important consideration in the performance of the Schick test is the integrity of the toxin. He related an incident showing the effect of a 50 mile drive over a colonial road in New Zealand with toxin already made up for injection. In the group of subjects on whom the Schick tests were done, 40 per cent were found to have positive reactions. On retests of the same group later, with material mixed at the place of using, an additional 40 per cent showed a positive reaction.

REACTIONS TO TOXOID

While reactions to toxoid have been reported, they have been encountered mostly in adults.[12] Ramon [8] stated that from 1 to 5 per cent strong reactions (especially local) had been the French experience. He added, "To date (August, 1928) more than a million injections of anatoxin have been made in France and with the exception of the slight reactions just mentioned, no serious incident or fatal accident has occurred."

In our series of 128 children who received toxoid, only one reaction was noted, which occurred in a 1 year old child who was allergic to veal broth. He reacted to the first injection with an urticaria involving the entire upper extremity on the side into which the injection was made. This reaction was definitely one to the protein contained in the medium employed for producing the toxin.

Several children had slight areas of redness around the point of injection. In no case was this regarded by the mother as sufficient to report, the information being subsequently elicited by direct questioning. Zingher [4] remarked on the relatively few reactions to toxoid in young children.

In Weinfeld's [12] group of adults into whom toxoid had been injected, fifteen of twenty adults with pseudoreactions to the Schick test had

12. Weinfeld, G. F., and Cooperstock, M.: Comparative Effects of Diphtheria Toxoid and Toxin-Antitoxin as Immunizing Agents, Am. J. Dis. Child. **38**:35 (July) 1929.

reactions to toxoid. Weinfeld attempted to relate such a reaction to an allergic constitutional make-up of the reactors. It is, therefore, interesting to note that in our series of one hundred and twenty-eight children there were fourteen cases of eczema, fifteen of seborrheic dermatitis, one of asthmatic bronchitis and one of hay fever. The presence, then, of an allergic make-up did not necessarily provoke a toxoid reaction in the preschool child.

TABLE 2.—*Comparative Study of Immunization with Various Materials*

Kind of Material	Number of Tests	Positive Reactions to Schick Test	Negative Reactions to Schick Test	Per Cent Immune
Horse serum toxin-antitoxin	361	78	283	78
Sheep serum toxin-antitoxin	101	30	71	71
Larson's ricinoleated toxin (1 dose)	10	4	6	60
New York State Board of Health toxin-antitoxin	15	2	13	86
Toxoid	128	2	126	98

SUMMARY AND CONCLUSIONS

Table 2 summarizes the results obtained with various materials in immunization against diphtheria.

The superiority of toxoid over other materials is strikingly demonstrated. In the preschool child, toxoid obtained from reliable sources offers the ideal method of diphtheria immunization, because (*a*) it gives a greater percentage of immunes than does toxin-antitoxin, and (*b*) it avoids serum sensitization.

Any program of diphtheria immunization should include proper performance of the Schick test.

The best age for diphtheria immunization with toxoid is about 1 year.

DEXTROSE TOLERANCE TESTS FOLLOWING LOBAR PNEUMONIA IN CHILDREN *

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In a previous paper we [1] have shown that in children after the cessation of a ketosis induced by a ketogenic diet, the carbohydrate metabolism does not return to normal at once but passes through a transitory stage. During this stage, there appears to be an excessive ability to utilize carbohydrates. This is shown by the occurrence of only a slight rise in the blood sugar curve in a dextrose tolerance test. The same low type of blood sugar tolerance curve is also seen following recovery from ketosis caused by cyclic vomiting.

Often during an acute lobar pneumonic infection in children acetone is found in the urine. According to Binger, Hastings, Sendroy, Neill and Morgan,[2] there is not a true ketosis during lobar pneumonia. They based their conclusions on the presence of normal blood reaction and normal blood gases. The constant occurrence of acetonuria in many acute infections of children, however, must be associated with some disturbance of carbohydrate metabolism. In order to ascertain the type of blood sugar curve that was present after the acetonuria of such an infection, children with lobar pneumonia were examined. Lobar pneumonia was selected because in such cases the patients usually have a crisis, and there is an abrupt transition from a febrile to a nonfebrile stage. It was thought that possibly these children would show the same low type of blood sugar curve as was obtained after the induced or spontaneous ketosis.

Eight children with lobar pneumonia were examined. The eight children, four boys and four girls, were from 3 to 12 years of age. The patients were all admitted to the pediatric service of Mount Sinai Hospital. During the attack of pneumonia, the children were treated in the usual manner; no specific serum was used in any of the cases.

* Submitted for publication, Oct. 28, 1929.

* From the Pediatric Service, Mount Sinai Hospital.

1. Kohn, J. L.; Fries, M. E., and Felshin, G.: Spontaneous and Induced Ketosis in Children, Am. J. Dis. Child. **34**:857 (Nov.) 1927.

2. Hastings, A. B.; Neill, J. M.; Morgan, H. J., and Binger, C. A. L.: Blood Reaction and Blood Gases in Pneumonia, J. Clin. Investigation **1**:25 (Oct. 20) 1924. Binger, C. A. L.; Hastings, A. B., and Sendroy, J.: A Further Study of the Blood Reaction and Blood Gases in Pneumonia, J. Exper. Med. **45**:1081 (June) 1927.

Fluids were given by mouth and consisted mainly of milk, orange juice and water, to which about 10 per cent of carbohydrate was added. No tolerance tests could be done during the febrile period, as the children were never really fasting. The urine was tested for acetone every day during the febrile and postfebrile period.

Soon following the crisis, the children were put on a prescribed diet. The diet consisted of about 60 per cent carbohydrate, 15 per cent protein and 25 per cent fat. During the postfebrile period a dextrose tolerance test was done and repeated every two or three days until the child was discharged from the hospital. The test was begun after an over night fast of fourteen hours. The children were kept in bed during their entire stay in the hospital. A micromodification of the Folin-Wu blood sugar method was used. Two tenths of a cubic centimeter of blood was obtained by pricking the finger. Samples of blood were taken previous to the ingestion of dextrose, and thereafter every half hour for two hours and a final sample after three hours, making six tests in all. Ingestion of other food or water was not permitted until the completion of the test. One of us analyzed the specimens the same afternoon. When possible, specimens of urine were collected at half hour intervals for three hours.

The amount of dextrose given was estimated in relation to the sitting height of the children squared; i. e., 0.0085 Gm. of dextrose per centimeter of the sitting height squared. If correlated with the weigth of the child, it averaged from 1.4 to 1.7 Gm. of dextrose per kilogram of body weight. From previous tests on 100 normal children, Fries and Kohn [3] found the sitting height more satisfactory than the weight, since the sitting height is in relation to the expected weight and to the surface area. The surface area is a more accurate basis for calculation in overweight and underweight children. For children of normal weight and stature, either method may be used as a basis for the amount of dextrose to be given.

The dextrose was given in a 30 per cent solution, to which was added a little lemon juice to make it more palatable. Chemically pure anhydrous dextrose was used, and the water was added just before ingestion.

RESULTS

When the dextrose tolerance test was done two days or more after the pneumonic crisis, the blood sugar curve was normal in all patients. When done sooner than two days after the crisis, a diabetic blood sugar curve was usually obtained; that is, the maximum blood sugar was higher than normal, and the blood sugar did not return to the fasting

3. Fries, M. E., and Kohn, J. L.: Glucose Tolerance Test in Children. Am. J. M. Sc. **170**:547 (Oct.) 1925.

Data Obtained in Cases Following Lobar Pneumonia

Case	Age in Years	Sex	Weight in Kg.	Sitting Height in Cm.	No. of Days Before Crisis	Tolerance Test			Acetone in Urine			Type of Tolerance Curve	Blood Sugar Percentage					
						Gm. Dextrose per Kg.	No. of Days After Crisis	Date of Test	Date Positive	Date Negative	No. Days Between Disappearance and Test		Fasting	½ Hour	1 Hour	1½ Hours	2 Hours	3 Hours
1	7	F	20.4	67	9	1.6	2	2/ 8	2/ 6	2/ 7	1	High normal	120	170	200	170	170	130
							4	2/10			3	Normal	110	160	200	140	140	130
							8	2/14			7	Normal	100	220	180	180	118	
2	3	M	14.5	58	9	1.5	0	2/ 6	2/ 6	2/ 8	—2	High normal	140	240	380	250	190	140
							4	2/10			2	Normal	120	220	170	140	120	
							8	2/14			6	Normal	100	150	164	168	...	65
3	3	F	14.6	56	6	1.7	2	3/ 1	2/27	3/ 1	0	Normal	120	124	170	170	130	
							4	3/ 3			2	Normal	108	140	170	196	120	
							6	3/ 5			3	Normal	106	140	160	148	90	90
4	6	F	16	57	10	1.7	2	4/ 7	4/ 2	4/ 3	4	Normal	80	130	160	140	140	100
							4	4/ 9			6	Normal	95	130	156	124	142	
							7	4/12			9	Normal	95	168	200	176	138	92
5	11	F	27.7	72	6	1.6	2	4/21	4/18	4/19	2	Normal	104	138	190	176	140	118
							6	4/25			6	Normal	110	168	130	158	130	104
6	9	M	28.5	71	9	1.4	1	5/23	5/24	5/26	1	High normal	90	140	180	180	130	130
							3	5/28			3	Normal	80	140	146	130	125	
							6	6/ 1			6	Normal	75	158	140	120	95	
7	7	M	25	61	7	1.2	1	11/30	11/29	11/30	0	High normal	78	170	200	190	194	150
							3	12/ 2			2	High normal	72	160	230	226	210	82
							8	12/ 7			7	Normal	100	184	140	100	96	
							10	12/ 9			9	High normal	85	160	200	180	160	
							16	12/15			15	Normal	95	200	180	110	110	
8	7	M	22.5	62	6	1.4	3	12/ 7	12/ 2	12/ 5	2	Normal	102	140	120	110	120	
							5	12/ 9			4	Normal	100	186	140	140	106	
							11	12/15			10	Normal	110	200	160	110	110	

level within three hours. The severity or length of the illness had no effect on the tolerance test. The blood sugar during fasting was usually within normal limits. It was never as low as during an induced ketosis. Within two days after the crisis, the urine never contained acetone. Acetone was usually present during the febrile period. Occasionally the acetone would disappear one or two days before the crisis.

COMMENT

Labbé and Gavrila [4] have shown that if dextrose tolerance tests are done on patients with lobar pneumonia a diabetic curve is obtained. In our patients, tolerance tests done after the crisis were found to be normal. In a previous study,[1] tolerance tests done after the cessation of the ketogenic diet or after recovery from cyclic vomiting showed a low type of dextrose tolerance curve. We attempted to explain the low blood sugar curve by the fact that following the restoration of a normal carbohydrate diet the tissue cells, especially the liver cells, may have an increased avidity for carbohydrates in order to replenish their depleted storage. During the infection with pneumonia the children were given a large amount of carbohydrate, and although acetone was present in the urine, the carbohydrate depletion was probably not as great as in the induced ketosis.

It is known that increased body temperature raises the basal metabolic rate, and therefore more carbohydrate is burned in order to carry on body functions. Freund and Marchand [5] and MacLean and Sullivan [6] have shown that neither the degree of pyrexia nor its duration has a constant effect on the subsequent dextrose tolerance test.

The possible effect of the disease itself on the carbohydrate metabolism must be considered. It was shown by Andresen and Schmidt [7] that after a severe case of scarlet fever or a bacillary dysentery the dextrose tolerance curve remains high for a week or more. MacLean and Sullivan [6] noted the same results following epidemic encephalitis. After diphtheria, Elkeles and Heimann [8] found a diabetic type of blood sugar curve for a long period after recovery from the disease. Labbé and Gavrila [4] believed that pneumonia does not injure the carbohydrate

4. Labbé, M., and Gavrila, S.: Le trouble glycorégulateur au cours des maladies infectieuses aigües, Arch. d. mal. de l'app. digestif. **16**:987 (Nov.) 1926.

5. Freund, H., and Marchand, F.: Ueber des Verhalten des Blutzuckers im Fieber, Deutsches Arch. f. klin. Med. **110**:120 (March 13) 1913.

6. MacLean, A. B., and Sullivan, R. C.: Dextrose Tolerance in Infants and in Young Children, Am. J. Dis. Child. **37**:1146 (June) 1929.

7. Andresen, J., and Schmidt, A.: Zur Frage des Blutzucker Spiegel bei Infektionskrankheiten, Klin. Wchnschr. **6**:213 (Jan. 29) 1927.

8. Elkeles, A., and Heimann, F.: Ueber Störungen im Kohlehydratstoffweschsel bei Diphtherie, Deutsches Arch. klin. Med. **155**:263 (June) 1927.

mechanism. We can confirm this statement. Although lobar pneumonia is an intense infectious process during the febrile stage, there is apparently no injury to the carbohydrate mechanism. The severity of the illness had no effect on the tolerance test.

CONCLUSIONS

1. Dextrose tolerance tests when done within two days after the crisis in lobar pneumonia are normal and remain normal.

2. Although acetone is found in the patients' urine during lobar pneumonia, blood sugar curves made within two days after the crisis are not low, in contrast to the observations in cases following cessation of an induced ketosis or recovery after cyclic vomiting.

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RENAL RICKETS *

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In recent years, considerable attention has been paid to a peculiar combination of chronic renal disease and deformity of the bones, known as "renal infantilism," renal dwarfism" or "renal rickets." Shipley and his co-workers and [1] Lathrop,[2] Hunt,[3] Parsons [4] and Duken [5] have reviewed the literature on this subject and contributed additional case reports.

Parsons, who has made the most extensive chemical study of this condition, has stated that the bone deformities are those of true low calcium rickets, which, according to the x-ray picture, should be classified into three types: (*a*) atrophic type, (*b*) florid type and (*c*) "woolly" type. The decrease of the calcium level of the blood may be absolute, as in one case reported by Parsons [4] in which it was diminished to 3.95 mg. per hundred cubic centimeters, or only relative; that is, the calcium value is normal but low as compared with the high phosphorus, which reached values of 16 mg. per hundred cubic centimeters. All of the investigators think that the primary cause of the diminished deposition of calcium in the bone is the inability of the kidney to excrete phosphate, which leads to elevation of the blood phosphorus, as noted by Marriott and Howland,[6] and depression of blood calcium. In addition to phosphate retention, blood nonprotein nitrogen and urea are found elevated. Lathrop [2] and Duken [5] studied the other inorganic constituents of the blood. Lathrop found a low carbon dioxide capacity and increase in the hydrogen ion concentration, that is, a true acidosis, which became decompensated shortly before death. Duken has made

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1. Shipley, P. G.; Park, E. A.; McCollum, E. V., and Simmonds, N.: Is There More Than One Form of Rickets? Am. J. Dis. Child. **23**:91 (Feb.) 1922.
2. Lathrop, W. F.: Renal Dwarfism, Arch. Int. Med. **38**:612 (Nov.) 1926.
3. Hunt, F. C.: Renal Infantilism: Report of a Case and a Review of the Literature, Am. J. Dis. Child. **34**:234 (Aug.) 1927.
4. Parsons, L. G.: The Bone Changes Occurring in Renal and Coeliac Infantilism and Their Relationship to Rickets, Arch. Dis. Childhood **2**:1 (Feb.) 1927.
5. Duken, F.: Spaetrachitis, Tetanie und chronische Schrumpfniere, Ztschr. f. Kinderh. **46**:114, 1928.
6. Marriott, McKim, and Howland, J.: Phosphate Retention as a Factor in the Production of Acidosis in Nephritis, Arch. Int. Med. **18**:708 (Nov.) 1916.

one complete study of the acids and base of the blood serum. He was able to show that the lowering of bicarbonate is due to a deficiency of base in the serum and not to the presence of unknown acids.

All authors have agreed that renal insufficiency is the cause of this condition. The renal insufficiency leads to an acidosis which is supposed to cause a mobilization of calcium from the bone, resulting in decalcification. As proof of the true rachitic nature of this condition, Howland's product Ca × P has been calculated for these cases. Owing to the increase in phosphorus, it was found well above 40, out of the zone of active or healing rickets. Parsons calculated the solubility product for $Ca_3(PO_4)_2$: p (Ca^{++}) $(PO_4^{\equiv})$ according to Holt in his case and found it to be 23.4, which is the normal value. Calculating the product from Lathrop's data, he obtained a figure of 24.3, which is compatible with active rickets. Lathrop does not recognize this condition as true rickets, because the Ca × P product exceeded 40. In the cases in which healing of the rickets occurred, as in Duken's case, the phosphorus slowly came down to normal and calcium showed higher values. This was not due to the antirachitic treatment which, according to the nearly unanimous opinion of observers, is useless in this condition, but to an improvement of renal excretion. Duken's case is especially interesting, because the patient showed evidence of tetany when admitted to the hospital. Tetany has been observed in other cases of renal rickets. Acidosis which, in Parson's opinion, is a protective mechanism against tetany, does not always prevent the occurrence of tetany. Duken has not determined the amount of free or ionized calcium. In Lathrop's case, in which tetany was not present, the ionized calcium was found to be normal in spite of the low total calcium. The quotient Ca/P was frequently found to be lower than 1.2 (György),[7] but tetany did not occur. In the light of these observations, the theory of the pathogenesis of tetany may need correction.

CASE REPORT

History.—R. D., a boy, aged 8 years, an American, belonged to a family that had had no chronic illnesses. The mother's pregnancy and labor were normal. He was a full term child, weighing 3.4 Kg. and was normal at birth, except for bilateral inguinal hernia. He was breast fed for three months, but did poorly, weighing only slightly more than his birth weight at 3 months. Supplemental feeding of whole milk, dextrimaltose and barley water with cod liver oil and orange juice were then given, and later cereals. The child improved but still remained under weight. He sat up at between 5 and 6 months, had his first tooth at 11 months, talked at 1 year and walked at 16 months. His diet had always been well balanced.

7. György, P.: Ueber den Gehalt des Blutserums an Kalk und anorganischem Phosphor im Säuglingsalter, Jahrb. f. Kinderh. **99**:1, 1922.

The child had whooping cough at 2 years of age, and scarlet fever complicated by bilateral purulent otitis media at 3 years of age. He had always been pale and subject to colds. At 3 years of age, he presented clinical evidence of rickets. Because of smallness in size (weighing only 12 Kg.) an endocrine disturbance was suspected by the family physician, and thyroid extract was tried, without benefit. At that time, the patient was subjected to enuresis, and his urine contained a small amount of albumin. When 3½ years of age, he developed erythema multiforme. One month later, he had lobar pneumonia at the base of the right lung. He was admitted to the St. Louis Children's Hospital for the first time on Jan. 25, 1925, for treatment because the pneumonia persisted. At that time, the erythrocyte count was only 1,744,000. He showed typical rachitic bone deformities, such as bossing of the parietal and occipital bones, rachitic rosary, pigeon chest, Harrison's groove and genu valga, and the urine showed a heavy trace of albumin. He remained in the hospital for two weeks, during which time he received five transfusions of citrated whole blood (total of 625 cc.). On discharge, the lungs were clear and the erythrocyte count was 3,000,000. The Wassermann and Pirquet tests were negative. The albuminuria persisted.

Second Admission.—The second admission occurred at the age of 5 years. The results of the physical examination were essentially the same as on discharge from the hospital. He was 94 cm. tall, weighed 13.2 Kg. and showed marked rachitic deformities. His red blood count was 2,620,000. The blood pressure was 90 systolic and 60 diastolic. The blood showed high phosphorus and urea contents with low calcium and carbon dioxide contents. The urine had a low fixed specific gravity, and the phenolsulphonphthalein excretion was less than 10 per cent in two hours. Roentgen examination showed rachitic changes of the bones and rudimentary sinuses. The patient remained in the hospital for one month, during which time he received 200 cc. of citrated whole blood. On discharge, he was placed on an alkaline ash diet, which was continued at home.

Third Admission.—His third admission occurred at the age of 7½ years, when he was readmitted because of convulsions. The results of his physical examination were essentially the same as on his previous admission. His height was 97.8 cm. and his weight 13.2 Kg. His blood pressure was 90 systolic and 50 diastolic. The red blood count was 1,500,000. The urine contained a heavy trace of albumin with fixed low specific gravity. He was given 200 cc. of citrated whole blood intravenously on Oct. 28, 1928. He developed slight bronchitis that lasted three days. On November 1, a metabolic study was begun. Roentgen examination of the long bones at this time showed increased density without change of outline in the epiphyses. The skull showed thickening as well as increased density. The patient was discharged on December 1. The alkaline ash diet was discontinued.

Fourth Admission.—He was readmitted two days later because of cold, cough and abdominal pain. The physical observations were the same as when he was discharged, except for the evidence of an acute rhinopharyngeal infection and bronchitis. On December 8, the child showed signs of uremia and an exacerbation of the bronchitis. He was given 250 cc. of citrated whole blood intravenously and 500 cc. of equal parts of dextrose (5 per cent) and Ringer's solution twice during the day. That evening he had a generalized convulsion which was controlled by magnesium sulphate, intramuscularly. Two days later he had more convulsions that required calcium chloride and magnesium sulphate intravenously. From that time on, he began to improve with the administration of sodium bicarbonate and Ringer's solution intravenously and transfusions of citrated whole blood, although

there developed bilateral otitis media that required myringotomy. His convalescence was steady, and he was discharged on Jan. 21, 1929.

Fifth Admission.—His fifth admission occurred on March 16. He had done well at home on an alkaline ash diet until the day before admission, when a transient divergent strabismus developed. On the day of admission, he had two convulsions lasting four or five minutes each. The physical observations were essentially the same as on his previous admission. The blood pressure was 96 systolic and 58 diastolic. The red blood cells numbered 1,750,000, and the urine showed a heavy trace of albumin. He was given 5 cc. of 25 per cent magnesium sulphate intramuscularly; five days later, he had a recurrence of the strabismus followed by convulsions. He was given 100 cc. of 1 per cent magnesium sulphate solution intravenously. He was given 1 Gm. of calcium lactate three times a day and 2 drops of a preparation of irradiated ergosterol in oil three times a day. He had no more convulsions. He was given 300 cc. of citrated whole blood intravenously on April 15, and was discharged on April 27. His weight at that time was 33¾ pounds (15.3 Kg.) and his height 99.1 cm.

For the study of the blood, the methods used by Hartmann,[8] Hartmann and Darrow[9] and Schoenthal[10] were employed. For the study of the urine, the methods were the same as those used by Schoenthal.[10] The urine was collected under oil, toluol added, and it was kept on ice. Calcium in the urine was determined by McCrudden's method.[11] Colorimetric phosphorus determinations on the urine was repeatedly checked by the phosphormolybdate method, and found to be accurate. For the determination of total base in the urine, phosphate was removed according to the method of Stadie and Ross.[12] The stools were dried with alcohol and preserved with thymol. Chloride was determined by Van Slyke's[13] method. Phosphorus was determined as phosphormolybdate. The phosphate of the stool was calculated at an assumed p_H of 7.4. Total sulphate was determined according to Benedict's[14] method. The values which were given are total sulphate. Calcium was determined by Aron's technic.[15] For the determination of the total base,

8. Hartmann, A. F.: Chemical Changes Occurring in the Body as a Result of Certain Diseases in Infants and Children: I. The Effect of Diarrhea, Vomiting, Dehydration and Oliguria on the Acid-Base Balance of the Plasma of Infants with Mastoiditis, Am. J. Dis. Child. **35**:557 (April) 1928.

9. Hartmann, A. F., and Darrow, D. C.: Chemical Changes Occurring in Body as a Result of Certain Diseases in Infants and Children: II. Acute Hemorrhagic Nephritis; Sub-Acute Nephritis; Severe Chronic Nephritis, J. Clin. Investigation **6**:127 (Aug.) 1928.

10. Schoenthal, L.: Acid-Base Metabolism: Effects of Administration of Salt and of Restriction of Water, Am. J. Dis. Child. **37**:244 (Feb.) 1929.

11. McCrudden, F. H.: The Quantitative Separation of Calcium and Magnesium in the Presence of Phosphates and Small Amounts of Iron for the Analysis of Foods, Urine and Feces, J. Biol. Chem. **7**:83, 1910.

12. Stadie, W. C., and Ross, E. C.: A Micro Method for the Determination of Base in Blood and Serum and Other Biological Material, J. Biol. Chem. **65**:735 (Oct.) 1925.

13. Van Slyke, D. D.: The Determination of Chlorides in Blood and Tissues, J. Biol. Chem. **58**:523, 1923-24.

14. Benedict, S. R.: The Estimation of Total Sulphur in Urine, J. Biol. Chem. **6**:363, 1909.

15. Aron, H.: Eine einfache Methode zur Bestimmung des Calciums im organischen Substanzen, Biochem. Ztschr. **4**:268, 1907.

0.1 Gm. of stool was ashed by the Neumann [16] method and the clear fluid made up with water to 25 cc. From 5 cc. of the filtrate, calcium was precipitated with ammonium oxalate. After centrifuging, the clear fluid was carefully decanted, phosphorus removed and continued as in the determination of total base in the blood.

Blood Chemical Changes.—The blood was first examined on Sept. 21, 1926. There were observed a low bicarbonate, a decrease in chloride, a normal or slightly low protein, high phosphate, slightly increased lactate, a low total base and total acid. The base-residue (B-R) or undetermined acid was not increased. The nonprotein nitrogen was greatly increased. The sugar was normal. The total osmolar concentration was at the upper limit of normal. Four examinations of the blood gave about the same picture; an increase in chloride was accompanied by a decrease

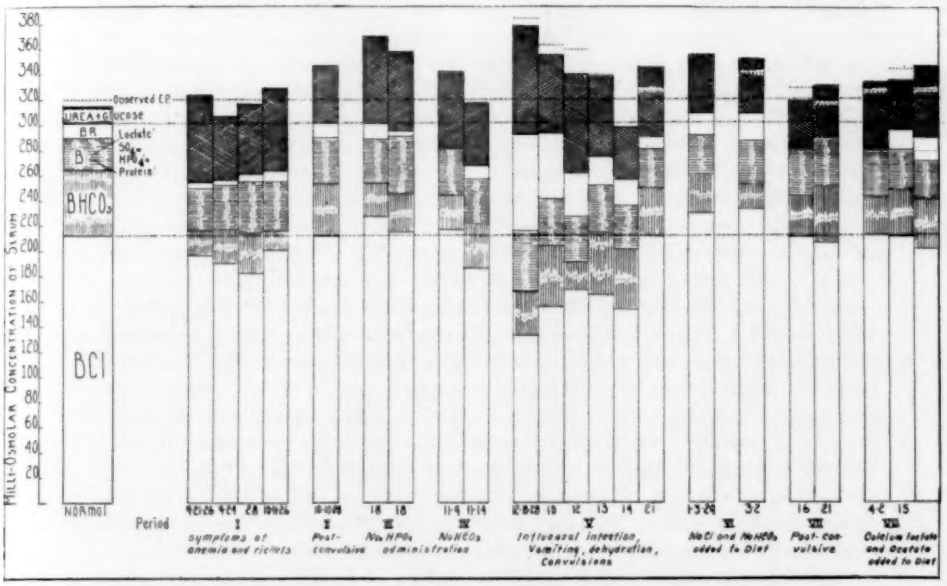

Chart 1 (Robert D.).—Case of renal insufficiency with rickets and infantilism.

in base bicarbonate. The total base did not go up to its normal value. Base bicarbonate was decreased, and the phosphate and sulphates were increased. At that time, blood transfusions were given, and the child was put on a diet which contained an excess of alkali.

When the child was readmitted to the hospital on Oct. 10, 1928, after about two years, the most striking feature was a normal total electrolyte concentration with an unchanged high nonprotein nitrogen content. The B-R was normal. The total osmolar concentration was increased to over 340 osmolar millimols and has been found increased ever since with one or two exceptions. At that period, the child was in fairly good condition but had a poor appetite. The temperature was normal. The effect of the addition of sodium bicarbonate to an analyzed diet will be discussed later. At that time, the child developed an influenzal infection

16. Neumann, A.: Einfache Veraschungsmethode, Ztschr. f. physiol. Chem. **37**:115, 1903.

(December 8) accompanied by vomiting, dehydration and convulsions; the chloride and bicarbonate were decreased, while there was an increase in protein due to the increased concentration of the blood. The phosphate and sulphate were high. There was a difference between the total base and the total acids as determined of 35.4 millimols. Corresponding to the high protein, the nonprotein nitrogen reached its highest value of 258 mg. The total osmolar concentration, as calculated, was increased to 379 osmolar millimols which agreed well with the observed, 385 osmolar millimols. The child was treated with Ringer's solution, dextrose and bicarbonate given intravenously and subcutaneously. After two days under this treatment, the water content was found to be 92.5. The protein of the serum was correspondingly decreased. The chlorides and bicarbonate increased, and phosphate, sulphate and lactate decreased. The total base remained the same. The B-R fell to 25 millimols. While dextrose increased, the nonprotein nitrogen decreased. The calculated osmolar concentration was still high (356 osmolar millimols) and agreed well with the observed 364 osmolar millimols. Only after thirteen days did the electrolyte concentration return to the values present before the onset of infection. With the disappearance of the B-R, the total base concentration reached as low values as 116 and 120 millimols, so that it is probable that together with the unknown acid, base was lost from the body. It was only after a normal B-R was reestablished that total base values came back to normal. The total osmolar concentration, however, remained well above the normal level.

Subsequently, sodium chloride and sodium bicarbonate were added to the diet in amounts of 5 Gm. of each daily. This led to an increase in the chloride concentration of the serum, while bicarbonate remained unchanged. The total base concentration was slightly increased. Phosphate, lactate and sulphate remained at the same level. The nonprotein nitrogen was increased so that the total osmolar concentration was well above normal (348, 342 osmolar millimols). In both instances, a p_H of 7.33 was observed.

Following several convulsions on March 16, 1929, the blood was studied again. The total osmolar concentration at that time was only slightly increased; the changes were in general, similar to those previously observed. Then, first, calcium lactate and two weeks later, calcium acetate 3 Gm. of each per diem, were added to the diet. This again produced an increase in the total osmolar concentration. The effect on the calcium and phosphorus will be discussed later.

The Calcium and Phosphorus in the Serum: It was of especial interest to follow the changes of calcium and phosphorus during this period of two and a half years. It appears from our data that there is no relationship between absolute height of protein and calcium. The globulin-albumin ratio was normal. The calcium values varied between 5.3 and 8.8 mg. per hundred cubic centimeters, being always below normal. The phosphorus was always increased, varying from 6.5 to 17.2 mg. per hundred cubic centimeters except after administration of calcium acetate, when it fell on a single occasion to 2.5 mg. per hundred cubic centimeters. Phosphorus and nonprotein nitrogen values nearly paralleled each other, while the trend of calcium values was in the opposite direction. The calcium-phosphorus product was found to be remarkably constant. It was always well above 40, and therefore far outside the zone of genuine active rickets. Only after calcium acetate had been given and the values of phosphorus had fallen did the product fall lower than 30.

Administration of Disodium Phosphate: Warkany[17] observed in infantile rickets that feeding of disodium phosphate, 0.5 Gm. per kilogram of body weight,

17. Warkany, J.: Die phosphataemische Kurve des normalen und des rachitischen Organismus, Ztschr. f. Kinderh. **46**:1, 1928.

failed to produce an increase in the phosphorus of the blood, as it did in normal infants. In agreement with Roeckemann and Stoffel,[18] he found that while in normal infants the phosphorus showed an average increase of 3 mg. per hundred cubic centimeters after two hours. there was only an average increase of 0.4 mg. in those suffering from manifest rickets. In our patient, after the administration of 8 Gm. of $Na_2HPO_4 + 12\ H_2O$, the phosphorus which showed a value of 7.8 mg. before the feeding, increased 0.9 mg. per hundred cubic centimeters after one hour and 1.5 mg. per hundred cubic centimeters after three hours. A repetition of this experiment under the same conditions, showed an increase of 1 mg. per hundred cubic centimeters, one hour and forty-five minutes after the salt was given. At the same time, the calcium showed a decrease, being reduced from 7.4 to 5.8 mg. per hundred cubic centimeters in the first experiment and from 7.3 to 6.9 mg. per hundred cubic centimeters in the second. In the second experiment, the phosphorus excretion in the urine was followed; 8 Gm. of $Na_2HPO_4 + 12\ H_4O$ corresponds to 0.695 Gm. of phosphorus or 0.045 Gm. per kilogram of body weight. The average phosphorus excretion in the urine before and after the experiment was 54 mg. in twenty-four hours. A calculation of the excess phosphorus excreted in the urine during the four days following the administration of disodium phosphate was 168 mg. The rise in serum phosphorus was 1.5 mg. per hundred cubic centimeters. If one calculates the increase of phosphorus for the whole body, taking two thirds of the body weight as body fluids, one obtains an increase of 150 mg. of phosphorus. This would indicate that there was a diminution in absorption of phosphorus from the intestinal tract and that the phosphorus which was absorbed was excreted through the urine only after four days. Renal insufficiency seems to be combined with the same disturbance of phosphorus absorption as does rickets.

In order to study the total acid base metabolism of this patient and the influence of alkali on the acid base and calcium phosphorus metabolism, the child was placed on an analyzed diet. This diet consisted of dried milk, oleomargarine, crackers, puffed wheat and orange juice. The fluid intake was kept constant. The daily food intake was not constant, but was accurately known for every day. The child was kept in bed. Complete specimens of the urine and of the stools were obtained. Vomiting did not occur.

During the first period of three days, the child took 850 calories per day; during the second period of five days, the child took only 410 calories. On the first and second day of the second period, 15 Gm. sodium bicarbonate were added to the diet; 10 Gm. on the first and 5 Gm. on the second day. It was calculated that 10 Gm. of sodium bicarbonate was just sufficient to restore the blood bicarbonate to a normal level.

(*a*) Blood Changes: A complete study of the blood was made before the orange juice containing the bicarbonate was given on Nov. 9, 1928. It can be seen from chart 1, that the blood chemistry at that time was the same as on the second admission on Oct. 11, 1928, the only difference of importance being that the total electrolyte concentration was lower as indicated by a lower value of the total base (136 cc. tenth-normal). The protein at that time was normal (7.88 Gm. per cent), 5.11 Gm. of which was albumin and 2.77 Gm. of which was globulin. Phosphorus was 7.7 mg. per cent, calcium 8.9 mg. per hundred cubic centimeters and the p_H 7.23. Three hours after the sodium bicarbonate had been given, bicarbonate was found to be increased from 12.5 to 21.6 cc. tenth-normal. Phosphorus showed an

18. Roeckemann, W., and Stoffel, R.: Die Beeinflussung der Anorganischem Serumphosphate durch orale Phosphatzufuhr, Ztschr. f. Kinderh. **41**:661, 1926.

increase of 1.3 mg. per hundred cubic centimeters. At the same time Ca was reduced from 8.9 to 6.9 mg. per hundred cubic centimeters. The nonprotein nitrogen was not changed. No signs of tetany could be found. On the next day, November 10, two hours after 5 Gm. of sodium bicarbonate had been given, chloride and bicarbonate were determined. The chloride was diminished. The bicarbonate was increased by only 4.5 millimols. On the last day of the experiment chloride was further reduced and bicarbonate remained at a higher level. The total osmolar concentration was reduced due to the decrease in chloride and the diminution of the nonprotein nitrogen from 200 to 160 mg. per hundred cubic centimeters. As a consequence of the calculation of osmolar concentration according to the ionization, it appears as if the total base were decreased after sodium bicarbonate was

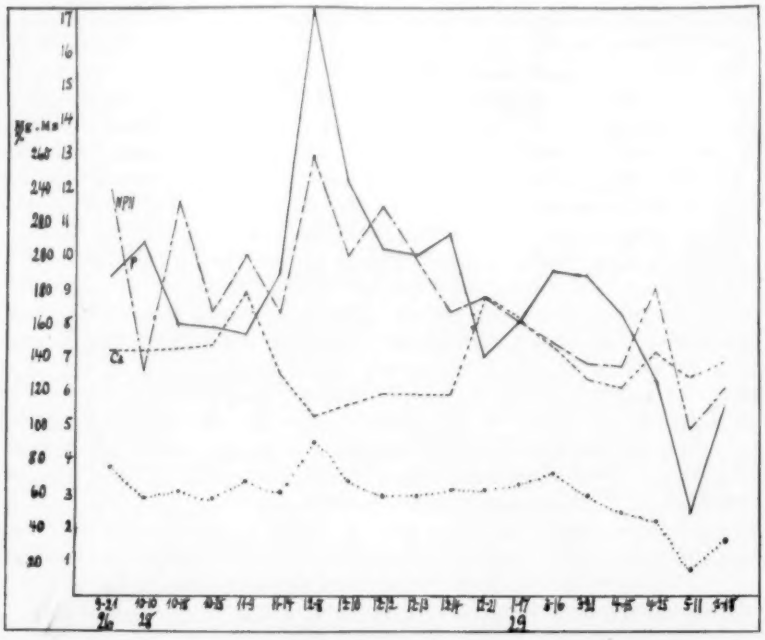

Chart 2 (Robert D.).—Calcium, phosphorus, nonprotein nitrogen and calcium phosphorus product during the period covered by chart 1: continuous line, protein; dash line, calcium; long dash-short dash line, nonprotein nitrogen; dotted line, calcium phosphorus products.

administered. After direct determination, however, the total base showed very slight increase of 4.8 cc. tenth-normal per hundred cubic centimeters as should be expected. Phosphorus remained increased to 9.5 mg. per hundred cubic centimeters, while calcium was reduced to 6.5 mg. per hundred cubic centimeters. The p_H was increased from 7.23 to 7.32 at the time of the experiment. The calcium phosphorus product showed values of 67.4 before and 61.7 after administration of sodium bicarbonate. These results appear in graphic form in chart 2.

(*b*) Urine: The excretion of acid and base during the time the child was on a fixed diet was followed. During the first period previous to alkali administration, all the values for acids and bases showed decrease following the reduction

of the food intake. In spite of the diminished output of urine, there was no change in the p_H. The excretion of organic acids was small but within normal limits. The ammonia excretion was very low; it did not reach one tenth of the base excretion. The ammonia coefficient remained constantly below 3. In contradistinction to the low ammonia values, the titrable acidity showed higher values. The total fixed base excretion paralleled the total acids, which, according to the p_H, exceeded the total of fixed base plus ammonium. Calcium excretion was always very low and did not follow the decrease of the other cations and anions. Nitrogen showed the same decrease as the other urinary constituents. After the administration of sodium bicarbonate, the urinary output increased despite a fixed fluid intake. There was no change in the p_H, nor did the bicarbonate output increase. All the urinary constituents except the bicarbonate showed an increase on the second day of this period. The organic acids did not exceed their values for the first period until the third day, when about 100 per cent more were excreted than during the first two days. There was no diacetic acid in the urine, nor

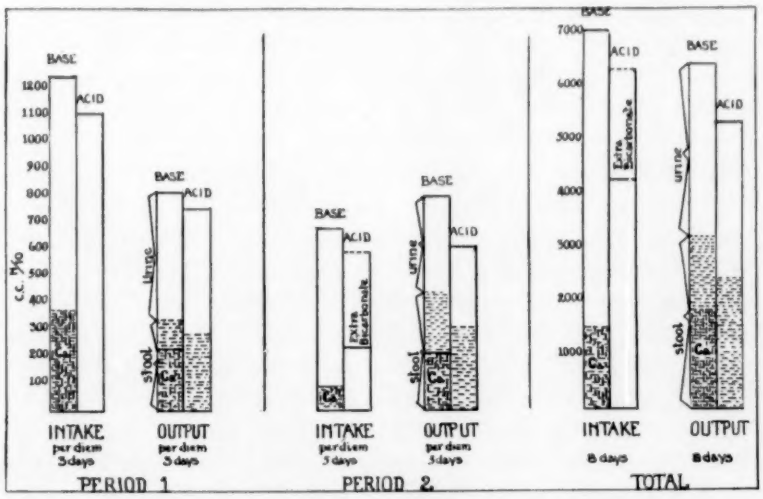

Chart 3.—Acid base balance in case R. D.

could we detect any acetone bodies in the blood. Again, there was no change in the ammonia coefficient. The calcium output in the urine was parallel to that of the fixed base.

(*c*) Stool: During the fore period of three days, the average daily amount of dried stool was 7.53 Gm. containing 13.7 cc. tenth-normal chloride, 213 cc. tenth-normal phosphate, 61 cc. tenth-normal sulphate and 216 cc. tenth-normal nitrogen, corresponding to a total of 288.7 cc. tenth-normal acid per day as compared with the calcium of 221 cc. tenth-normal and a total fixed base of 314 cc. tenth-normal. Therefore, 74 per cent of the fixed base consisted of calcium.

During the second alkali period, the average daily amount of dried stool was 9.92 Gm. and contained 16 cc. tenth-normal chloride, 237 cc. tenth-normal phosphate, 59 cc. tenth-normal sulphate and 316 cc. tenth-normal nitrogen. The total fixed acids amounted to 319 cc. tenth-normal. The total base amounted to 441 cc. tenth-normal, 211 cc. tenth-normal or 48 per cent of which was calcium. There was a much larger excess of base over acid during the second period. From the

lower percentage of calcium in the second period, it might be concluded that if alkali as sodium was available, less calcium was excreted through the bowel. On the other hand, the excess of base which was not calcium during the second period might be due to an insufficient absorption of bicarbonate from the intestinal tract.

(*d*) Total Balance: In comparing the total intake and output, there was a positive total acid, total base and calcium balance during the first period. The nitrogen and phosphorus balance was negative during this time. The negative phosphorus balance was chiefly due to the larger excretion through the bowel. During the second period after further reduction of the food intake, all the inorganic constituents involved in rectal and urinary excretion showed a negative balance. It is remarkable that the total base excretion per diem remained the same in spite of changes in the food intake. The same was true for the calcium, the loss of which was entirely due to excretion by way of the bowel. If, however, the two periods are considered together, a positive base balance is found to be present. In contradistinction to the positive base balance, there was a negative calcium balance for the whole period. This indicates that a depletion of calcium can take place without an impairment of the base equilibrium or alkali reserve of the body. The phosphorus and nitrogen balances for both periods were negative. The results are illustrated graphically in chart 3.

COMMENT

The case described may safely be considered as one of renal rickets on the basis of clinical history, roentgen examination and chemical observations. The renal condition appears to have been present in very early life and may possibly have been congenital. Clinical evidence of rickets was present in early infancy. The case, therefore, is of the type described by Parsons (case 2),[4] Fletcher,[19] Miller and Parsons,[20] Porter,[21] Patterson[22] and Hunt,[3] in which the disease was present in early life. This type of case differs from the type that occurs toward the end of the first decade of life or at the time of puberty, as in Lathrop's case and in Parson's cases 4 and 5. The bony changes are different, depending on the time of onset. Unfortunately, no x-ray pictures were taken during infancy, in our case, so that the diagnosis of early rickets rests entirely on clinical observations of a number of physicians who had, from time to time, treated the child. At the age of 8, only three metacarpal bones were present.

Our investigation has been concerned chiefly with a study of the metabolism of the substances involved in the maintenance of the acid-base equilibrium and in bone formation. It has been shown that loss

19. Fletcher, M.: Case of Infantilism with Polyuria and Chronic Renal Disease, Proc. Roy. Soc. Med. **4**:95, 1911.

20. Miller, R., and Parsons, L.: Renal Infantilism, Brit. J. Child. Dis. **9**:289, 1912.

21. Porter, L.: Renal Infantilism, Arch. Pediat. **32**:85, 1915.

22. Patterson, D. H.: Three Cases of Renal Dwarfism Associated with Curious Bony Changes, Case 2, Proc. Roy. Soc. Med. **13**:107 (June) 1920.

of base as a result of diminished food intake could be prevented to a certain degree by addition to the diet of sodium bicarbonate. This loss could be prevented to a certain degree during periods of infection by parenteral administration of dextrose, Ringer's solution and sodium bicarbonate. The blood of the patient showed the typical observations of chronic renal insufficiency: normal or low total base, low bicarbonate, low protein, low calcium, high phosphate and high nonprotein nitrogen. The lactic acid of the blood was high only after convulsions. The total osmotic concentration exceeded normal limits. During the time when the patient was in coma, the B-R of the body fluids greatly exceeded the normal. The latter pointed to the presence of an unknown acid which disappeared coincident with clinical improvement. Except for this one period, the B-R was essentially normal, so that the acidosis was to be attributed primarily to loss of base from the body and not to the presence of an abnormal acid. It would appear that the presence of substances capable of binding calcium was responsible for the failure of normal ossification. One substance which was probably responsible for the binding of calcium was phosphate, which, due to renal insufficiency, was retained in high concentration. It is well known that in the presence of renal insufficiency more fixed base is necessary for excretion than under ordinary conditions. In spite of the observed loss of calcium and phosphate, it would be difficult to find a satisfactory explanation for the rachitic changes, as loss of calcium and phosphorus from the body does not in itself produce characteristic rachitic changes. It might be assumed in this case that the infant suffered from genuine rickets in early infancy and that these changes were persistent, due to the altered metabolism, leading to failure of calcium deposition. The observations in our case fail to explain the occurrence of rickets on the basis of the supersaturation theory, for a calculation of the solubility product for basic calcium phosphate (Holt) [23] or for calcium phosphate acid (Shear and Kramer) [24] gives a figure outside of the zone of active rickets. It is of course possible that the calcium may not have been present in a sufficient amount in ionized form, but that its ionization may have been interfered with as a result of the altered composition of the blood. We have no figures on the degree of calcium ionization in our case. Certainly, protein could hardly have been a factor as this was not present in increased amounts, and the albumin-globulin ratio was normal.

23. Holt, L. E., Jr.; LaMer, V. K., and Chown, H. B.: Studies in Calcification, J. Biol. Chem. I **64**:509 (July) 1925; II **64**:567 (July) 1925; III **64**:579 (July) 1925.

24. Shear, M. J., and Kramer, B.: Composition of Bone: III. Physicochemical Mechanism, J. Biol. Chem. **79**:125 (Sept.) 1928.

CONCLUSIONS

Two types of renal rickets may be distinguished: one, due to congenital malformation of the kidney or urinary tract; another, due to a chronic renal insufficiency of the character of a chronic interstitial nephritis becoming manifest later in childhood.

Detailed metabolic studies on a case of the first type, in a child aged 8 years, showed a negative total base balance, a negative calcium balance and a negative phosphate balance during certain periods. The blood changes were a moderately low total base, low bicarbonate, low protein, low calcium, high phosphate and high nonprotein nitrogen; both calculated and observed osmotic concentrations exceeded the normal. Chronic acidosis was present over a long time.

Disodium phosphate administered to this patient was poorly absorbed and slowly excreted and resulted in a lowering of blood calcium with but a slight increase in blood phosphate. The effects were similar to those observed in genuine rickets.

Sodium bicarbonate, administered by mouth, led to a positive base balance, although the calcium balance remained negative. The loss of calcium was chiefly by way of the bowel. The effect on the blood was an increase in phosphate, a decrease in calcium and an increase in the bicarbonate and total base.

Calcium acetate, when administered by mouth, led to a decrease in blood phosphate and a slight increase in blood calcium. There was no appreciable effect on the bicarbonate or total base.

The usual methods of treatment of rickets, such as the administration of vitamin "D" are ineffective in the case of renal rickets. Replacement of the depleted base, calcium and phosphate, is a logical method of treatment, although the effects are but temporary unless the treatment is continuous. This may be accomplished by the administration of an alkaline ash diet, together with calcium acetate.

THE TREATMENT OF ERYSIPELAS IN INFANTS

REPORT OF THIRTY-THREE CASES TREATED WITH ANTISTREPTOCOCCUS (ERYSIPELAS) SERUM *

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In any disease in which the mortality rate is unusually high, numerous and not altogether successful methods of treatment are likely to be advocated. This has been true of erysipelas in infants. Morse [1] reported 90 per cent mortality in infants; Erdman [2] reported 39.7 per cent; while Schaffer and Rothman [3] gave the following results: infants under 1 month of age, 80 per cent; under 6 months, 53 per cent; from 6 to 12 months, 47 per cent, and from 1 to 2 years, 14 per cent. As regards the influence of different forms of therapy, Knox [4] reported a mortality rate of 60 per cent in infants under 6 months of age treated by local measures; Robertson [5] quoted 65 per cent in infants under 12 months of age treated by exsanguination-transfusion; Borovsky,[6] 29 per cent by the use of a 2 per cent solution of mercurochrome-220 soluble applied locally and accompanied by citrated blood intramuscularly. Schaffer and Rothman [3] reported a decrease in mortality in nineteen patients who were given whole blood intravenously. From these reports one may readily see that the high mortality rate of erysipelas has not been reduced remarkably and that the various methods of treatment suggested have been far from satisfactory.

Rivers,[7] in 1925, produced erysipelas-like lesions in rabbits with hemolytic streptococci isolated from a human case of erysipelas, and

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* From the Infants' and Children's Hospitals and the Department of Pediatrics, Harvard Medical School.

1. Morse, J. L.: Clinical Pediatrics, Philadelphia, W. B. Saunders Company, 1926.

2. Erdman, S.: Erysipelas, J. A. M. A. **61**:2048 (Dec. 6) 1913.

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4. Knox, J. H. M., Jr.: Erysipelas in Childhood, South. M. J. **14**:287, 1921.

5. Robertson, L. B.: Exsanguination Transfusion: New Therapeutic Measurement, Treatment of Severe Toxemias, Arch. Surg. **9**:1 (July) 1924.

6. Borovsky, M. P.: Treatment of Erysipelas in Infants, Arch. Pediat. **44**:53, 1927.

7. Rivers, T. M.: Skin Infections of Rabbits with Hemolytic Streptococci Isolated from a Patient with Erysipelas: Method of Demonstrating Protective Action of Immune Serums, J. Exper. Med. **41**:179, 1925.

also produced an immune serum capable of protecting the skin of these animals against the injurious action of the same organism. In the same year, observations in experimental erysipelas were also published by Amos and Birkhaug.[8] In 1926, Birkhaug [9] published the results obtained by treating sixty patients with an antitoxin produced by using the toxic products of a specific strain of streptococci derived from patients suffering from this disease. The patients so treated showed definite clinical improvement with amelioration of the degree of toxicity, a critical fall in temperature, a reduction in pulse rate and a rapid subsidence of the lesion. Following the use of antistreptococcus (erysipelas) serum, reports of success and of failure appeared in the literature.

In 1927, Symmers and Lewis [10] reported 131 consecutive cases of erysipelas occurring in adults, who were treated at the Bellevue Hospital, New York, by the use of antitoxin. They concluded that the antitoxin was of definite value both as a therapeutic measure and as an economic procedure. Again in 1928, they [11] reported 705 consecutive cases in which a similar method of treatment was used, and again they arrived at the same conclusions and stated that their mortality rate was reduced from 11.2 per cent in untreated patients to 5.3 per cent in treated patients. Allen and Wilder [12] have reported similar results from Toronto. McCann,[13] however, was unable to confirm the results as obtained by others, and concluded that the antitoxin is of questionable value.

The published statistics in a large degree dealt with adults, or with groups of different ages in whom the mortality rate is not high, and in whom reduction may be due to many extraneous factors. Many of the factors that may influence the mortality rate in adults are singularly absent in infants, and therefore it would appear that the use of a specific serum in this group of patients would be a more accurate method of

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8. Amos, H. L., and Birkhaug, K. E.: Observations in Experimental Erysipelas, Tr. A. Am. Phys. **40**:5, 1925.

9. Birkhaug, K. E.: Erysipelas: Etiology and Treatment with Erysipelas Anti-Streptococcus Serum, J. A. M. A. **86**:1411 (May 6) 1926.

10. Symmers, D., and Lewis, K. M.: Erysipelas Antitoxin: Observations on One Hundred and Thirty-one Patients at the Bellevue Hospital, J. A. M. A. **89**:880 (Sept. 10) 1927.

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12. Allen, F. N., and Wilder, R. M.: Erysipelas Antitoxin, M. Clin. N. Amer. **11**:1653, 1928.

13. McCann, W. S.: Serum Treatment of Erysipelas, J. A. M. A. **91**:78 (July 14) 1928.

determining its true efficacy. This report concerns the results of treatment with serum in thirty-three infants.

METHOD

The method employed in the administration of the serum was as follows:

In the average case, 10 cc. of the serum (concentrated form) was given intramuscularly at the time of admission and daily thereafter as long as the lesion persisted. However, in the more desperate cases, as when the patients admitted were in a moribund condition, the initial dosage was given intravenously (the unconcentrated form) and the subsequent treatments intramuscularly. It may be well to mention at this point that no immediate untoward reactions were observed following the intravenous therapy.

As mentioned in the preceding paragraphs, the serum was given daily as long as the lesion persisted; therefore, the number of treatments varied according to the severity of the case. In a few cases only two or three injections were necessary, but usually from six to eight were given before there was a complete subsidence of the infection. Patients who were so unfortunate as to have a recurrence of the infection were given a second course of treatment.

TABLE 1.—*Patients Treated*

	Within 72 Hours of Onset	After 72 Hours
Number of cases	19	14
Average days of illness	2.1	5.93
Number of complications	13	14
Average duration of temperature	4.12	5.83
Number of recurrences	2	0
Patients with serum rash	9	0
Average number of treatments	5.26	..
Number of deaths	3	9
Number recovered	16	5

COMMENT

The results obtained in the treatment of thirty-three patients with cases of erysipelas are presented in detail in the tables.

Five patients were admitted to the hospital within twenty-four hours of the onset of the infection, and of those five, one died; a mortality rate of 20 per cent. This patient had eczema, pneumonia and septicemia at the time of admission. Seven patients were admitted within forty-eight hours of onset, and all recovered. Seven were admitted within seventy-two hours of onset and of this group two died, a mortality rate of 28.57 per cent. Both patients who died presented severe complications at the time of admission. Fourteen patients were admitted after seventy-two hours of illness and nine died, a mortality rate of 64.28 per cent. These results clearly illustrate the importance of early diagnosis and treatment.

One of the earliest signs of improvement following the administration of the serum was the disappearance of evidences of toxicity as

TABLE 2.—*Patients Treated Within Seventy-Two Hours After Onset*

Age	Sex	Day of Illness	Involvement	Temperature on Admission, F.	Day of Normal Temperature	White Blood Cells	Blood Culture	Amount (Cc.) and Method of Injection of Serum*	Number of Treatments	Serum Rash Day	Complications	Result	Comment
9 mo.	F	1	Face	101.6	2	40,000	.....	40 i-m.	4	8	None	Recovery	Lesion spread for following 24 hours; rapid recovery
3 mo.	F	3	Body	102.8	..	26,400	Negative	50 i-m.	5	..	Pneumonia, abscess, cellulitis	Death on 5th day	Admitted in extremis
13 mo.	F	3	Face	104	4	28,000	Negative	40 i-m. 90 i-m.	14	10	Recurrence	Recovery	Recurrence on 11th day with rise in temperature to 105 F.; 9 treatments followed
2 wk.	F	3	Legs	104.6	5	15,000	Negative	70 i-m. 50 i-m.	12	8	Recurrence, abscess	Recovery	Recurrence on 10th day; 5 more treatments given
8 mo.	M	1	Face	102	3	27,000	Negative	7 i-m.	1	0	None	Recovery	Mild form
5 mo.	F	3	Leg	104	3	15,700	Negative	21 i-m.	3	0	None	Recovery	Rapid recovery; moderate extension
23 mo.	M	2	Legs	103.6	5	30,700	Negative	45 i-m.	5	0	None	Recovery	Lesion spread over buttocks and abdomen
3 wk.	F	2	Half of face and scalp	104	6	26,000	Negative	65 i-v.	6	0	Cervical adenitis, parotitis	Recovery	Parotitis secondary to erysipelas; extremely toxic on admission
11 mo.	M	3	Scalp and face	105.2	5	15,700	.....	40 i-v.	4	7	Bilateral otitis, cervical adenitis	Recovery	Complications present on admission
8 mo.	M	1	Leg	104	..	16,600	Pneumococcus	8 i-m. 3 i-v.	2	..	Eczema, septicemia, pneumonia	Died on 5th day after admission	Complications present on admission; in extremis
8 wk.	M	2	Legs and buttocks	103.4	7	43,000	.....	25 i-m.	5	7	None	Recovery	Moderate extension of lesion
6 mo.	F	2	Feet and lower leg	103	4	22,000	Negative	40 i-m.	4	6	None	Recovery	Mild case
7 mo.	M	1	Cheek	103	2	24,400	Negative	10 i-m.	1	0	None	Recovery	Mild case
7 mo.	M	3	Face and scalp	104	..	28,000	.....	80 i-m.	8	9	Pericarditis with effusion, pneumonia	Death on 16th day	Complications present at time of admission
11 mo.	F	2	Left side of face	103	3	16,000	Negative	50 i-m.	5	0	None	Recovery	Rapid improvement
20 mo.	M	2	Face	105.6	3	17,500	Negative	35 i-m.	3	0	None	Recovery	Lesion spread over entire face
13 mo.	M	1	Face, neck and scalp	103	6	9,600	Negative	50 i-m.	5	0	None	Recovery	Finally involved entire scalp
13 mo.	M	2	Leg below the knee	103.6	6	8,500	Negative	70 i-m.	6	7	None	Recovery	Lesion spread over entire leg
10½ mo.	F	3	Vulva	102.6	12	23,000	Negative	60 i-m.	6	7	Pharyngitis	Recovery	Return of temperature to normal delayed by infection of upper respiratory tract

* i-m. indicates intramuscular and i-v., intravenous.

TABLE 3.—*Patients Treated Seventy-Two Hours After Onset*

Age	Sex	Day of Illness	Involvement	Temperature on Admission, F.	Day of Normal Temperature	White Blood Cells	Blood Culture	Amount (Cc.) and Method of Injection of Serum*	Number of Treatments	Serum Rash Day	Complications	Result	Comment
6 mo.	M	8	Body	103.8	10	43,000	Negative	30 i-v. 40 i-m.	8	0	Pneumonia, empyema, abscess	Death on 5th day	
13 mo.	F	4	Leg and buttocks	101	2	50,000	.....	2 i-v.	1	0	None	Recovery	Immediate response
3 mo.	M	4	Scalp and face	103	6	18,000	.....	4 i-m.	1	0	None	Recovery	Marked improvement
12 mo.	F	10	Leg	105	..	21,200	Negative	5 i v. 70 i-m.	8	11	Peritonitis	Death on 17th day	Lesion covered body; operation; death 24 hours later
3 wk.	M	4	Entire body	103.8	..	21,000	Streptococcus hem. (2)	22 i-v. 8 i-m.	3	..	Otitis media	Death, 48 hours	In extremis
4 wk.	M	5	Face	104	..	.....	.....	.....	..	..	.....	Death, 4 hours	In extremis
4 wk.	M	4	Body and face	101	..	32,000	Negative	20 i-m.	2	0	Empyema, mediastinitis, infected cephalohematoma	Death, 24 hours	
17 mo.	M	5	Scalp and neck	104	9	14,800	Negative (2)	90 i-m. 169 i-v.	12	..	Pneumonia, abscess	Recovery	Extremely ill; recurrence on 5th day
4 wk.	F	5	Legs, abdomen, back and buttocks	102	..	15,000	Streptococcus hem. (2)	40 i-v. 20 i-m.	3	..	Abscess, septicemia	Death, 48 hours	
16 mo.	M	4	Legs	104.6	4	12,800	Negative (2)	80 i-m.	8	6	None	Recovery	Rash spread rapidly
3 wk.	F	14	Trunk	103	..	7,900	Negative	10 i-m.	1	0	None	Death, 24 hours	
5 wk.	M	4	Face and neck	104	4	26,000	Negative	15 i-m.	2	0	None	Recovery	Rapid spread; good recovery
6 mo.	F	8	Trunk and legs	102	..	23,000	Negative	26 i-m.	3	0	Peritonitis	Death	In extremis
3 wk.	M	4	Head and face	100	..	27,000	Negative	75 i-v.	3	0	Pneumonia	Death 4th day	

* The serum used was either Mulford's or Squibb's; i-m. indicates intramuscular and i-v., intravenous.

manifested by their general appearance. This observation was quite consistent in all of the patients treated.

As shown in the tables, the extent of the lesion is not always altered, for in several of the patients the lesion gradually involved the entire body. Even in such conditions with continued extension of the lesion, the general constitutional state remained improved.

Patients who were treated within the first few hours of illness showed the most marked improvement, a fact which illustrates the importance of early administration of the antitoxin. Those patients who were treated late in the course of the disease showed only slight, if any, improvement. These observations are comparable with those reported by myself,[14] and Weldon[15] in the use of antitoxin in the treatment of

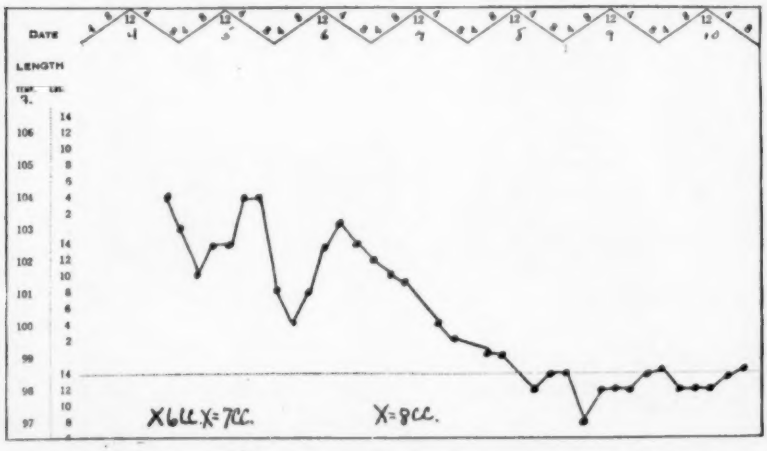

Chart 1.—Effect of Birkhaug's antitoxin on temperature. *X* indicates the intramuscular injection of the antitoxin to a patient 5 months of age. There was a complete recovery. The lesion involved the leg and thigh with advancement to the ilium.

patients with scarlet fever, in which it was shown that to be of value the antitoxin must be given early in the course of the disease.

Recurrences occurred in two patients, both of whom made good recoveries following a second course of antitoxin.

Positive blood cultures for hemolytic streptococcus were obtained in two patients, both of whom died. A pneumococcus septicemia occurred in one patient.

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14. Eley, R. C.: Scarlet Fever Antitoxin: Report of Four Hundred and Sixty-Five Cases, Am. J. Dis. Child. **35**:14 (Jan.) 1928.

15. Weldon, N. T.: The Use of Scarlet Fever Antitoxin, Am. J. Dis. Child. **37**:553 (March) 1929.

A serum rash occurred in twelve patients, the average day of appearance being 7.3. Usually the rash was not severe and was easily controlled by epinephrine and the local application of soothing lotions to the skin.

As can be seen from the tables, the average duration of a high temperature in patients treated within seventy-two hours of onset was 4.12 days in contrast to 5.83 days in those treated after seventy-two hours. In many of the patients who were treated early there was an abrupt fall in the temperature. This fall by crisis occurred with sufficient regularity to warrant being considered as a direct result of the antitoxin. The temperature curves shown in charts 1 and 2 illustrate this point.

Chart 2.—Effect of Mulford's antitoxin on temperature. *X* indicates the intramuscular injection of the antitoxin to a patient 6 years of age. *XX* indicates the intravenous injection of the antitoxin. The recovery was complete. The lesion involved the foot with advancement to the leg and thigh.

CONCLUSIONS

1. Antistreptococcus erysipelas antitoxin is of definite value as a therapeutic measure in the treatment of infants.

2. It must be given within the first seventy-two hours of illness in order that the optimum effects may be obtained.

3. The most noteworthy and consistent effect was the disappearance of toxicity, with general constitutional improvement.

HIGH PHOSPHORUS CONCENTRATIONS IN INFANTILE TETANY

A REPORT OF TWENTY CASES, WITH A REVIEW OF THE LITERATURE *

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Infantile tetany has been recognized as a clinical entity for many years, but Howland and Marriott [1] in 1918 were the first to describe its characteristic blood chemistry. They showed that the calcium content of the serum was greatly reduced in the active stages of tetany. Kramer, Tisdall and Howland [2] found that electrical reactions typical of tetany (the cathodal opening contraction less than 5 milliamperes and the anodal opening contraction less than the anodal closing contraction) were present when the calcium content of the serum was less than 7.5 mg. per hundred cubic centimeters. Little attention has been paid to the inorganic phosphorus content of the serum in tetany, as that has generally been reported to be at or slightly below the normal level. Thus in 1921 Kramer, Tisdall and Howland [2] reported normal values in seven cases of infantile tetany. Hess [3] and his co-workers in 1923 determined the inorganic phosphorus of the serum in sixteen cases of active tetany, and in no instance did they find it elevated above the normal level.

It is our purpose in the present paper to call attention to the occasional case of infantile tetany in which the inorganic phosphorus content of the serum is distinctly above the normal level. A survey of the literature would indicate that this is a comparatively infrequent accompaniment of tetany but that it undoubtedly does occur. Freudenberg and György [4] at the Heidelberg Clinic examined 300 cases, in five of

* Submitted for publication, Aug. 8, 1929.

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1. Howland, John, and Marriott, W. McKim: Observations upon the Calcium Content of the Blood in Infantile Tetany and upon the Effect of Treatment with Calcium, Quart. J. Med. **11**:289, 1918.

2. Kramer, B.; Tisdall, F. F., and Howland, J.: Observations on Infantile Tetany, Am. J. Dis. Child. **22**:431 (Nov.) 1921.

3. Hess, J. H.; Colvin, J. R.; Wang, Chi Che; and Fletcher, A.: Calcium and Phosphorus Determinations in the Blood Plasma in Rickets and Tetany, Am. J. Dis. Child. **26**:271 (Sept.) 1923.

4. Freudenberg, E., and György, P.: Ueber den gegenwärtigen stand des Problems der Säuglingstetanie, Ztschr. f. Kinderh. **44**:128, 1927.

TABLE 1.—*Cases of High Phosphorus Tetany Reported in the Literature*

Author	Case No.	Age, Mo.	Convulsions	Grouping of Symptoms*	Date	Blood Chemistry: Calcium, Mg. per 100 Cc. Serum	Blood Chemistry: Phosphorus, Mg. per 100 Cc. Serum	Treatment	Comment
Kramer, Tisdall and Howland... (footnote 2)	...	11	.....	.....	2/16/21	7.0	7.0		
Freudenberg and György..... (footnote 4)	1	..	.....	.....	.....	6.5 8.6	6.9 3.2	Ammonium chloride and sunlight	
	2	..	.....	.....	.....	6.7 9.1	6.9 5.6	Ammonium chloride and sunlight	
	3	..	.....	.....	.....	5.5 6.8	7.8 6.1	Ammonium chloride and sunlight	
	4	..	.....	.....	.....	6.9 5.6	6.8 7.5	Ammonium chloride and sunlight	
	5	..	.....	.....	.....	5.4 5.8	6.0 6.1	Ammonium chloride and sunlight	
Scheer and Salomon..... (footnote 5)	1	11	++++	Chvostek +++ Crow +++ Peroneal +++ COC 2.0	1/18/23 1/20/23 2/12/23 2/19/23	... ...	11.3 8.2 7.5 6.0	Hydrochloric acid milk and calcium chloride	Serum calcium was never lower than 8 mg. per 100 cc. of serum
	2	4½	++++	Crow ++++	.....	8.4	11.25	.....	Died soon after admission to hospital
Scott and Usher..... (footnote 6)	...	2	++++	Chvostek + Crow + Peroneal + Trousseau + COC 4.5	.....	9.6	6.3		
Hoag ..... (footnote 7)	1	5	.....	Chvostek + Crow + Trousseau ± Peroneal ± AOC < ACC COC 2.5	5/ 4/23 5/11/23 5/17/23	5.4 7.7 9.7	6.4† 10.3 6.2	Ultraviolet irradiation	All signs of tetany had disappeared by 5/17/23. CCC 3.5; COC 7.5+; ACC 7.0; AOC 7.5+
	2	12½	++++	Chvostek +++ Crow +++ Peroneal + Trousseau ± AOC < ACC	5/10/23 5/14/23 5/18/23 5/28/23	5.9 7.9 ... 9.7	8.1 6.4 6.8	Ultraviolet irradiation	No symptoms of tetany after 5/18/23
Powers ..... (footnote 8)	...	7 weeks	++++	Chvostek + COC 2.0; COC>5,ACC 3.0; AOC 2.5	..... 2 weeks later	5.9 5.3	8.8 10.8	Calcium chloride	Recovered
Tezner ..... (footnote 9)	...	5	++++	Chvostek + Trousseau + COC > 5	3/ 7/26 3/10/26	7.0 8.7	7.5 7.1	Strontium chloride	Recovered

* In this table and in table 2, COC indicates cathodal opening contraction; AOC, anodal opening contraction; CCC, cathodal closing contraction; ACC, anodal closing contraction.

† Phosphorus content of whole blood, Bell-Doisy method.

TABLE 2.—*Analysis of Twenty Cases of High Phosphorus Tetany*

Name	Age, Mo.	Cod Liver Oil Treatment Before Admission	Convulsions	Severity of Complications	Grouping of Symptoms	Date	Blood Chemistry: Calcium, Mg. per 100 Cc. Serum	Blood Chemistry: Phosphorus, Mg. per 100 Cc. Serum	Treatment After Admission	Outcome
J. S.	2	—	+	++	Chvostek ?	4/14	5.3	7.8	Ammonium chloride; calcium chloride; calcium lactate; ultraviolet irradiation	Recovered in twenty days
						4/17	6.9	5.3		
						4/20	5.3	5.6		
						4/25	9.2	—		
						5/ 3	8.1	3.7		
						5/12	10.3	4.7		
D. P.	9	—	+	++++	Chvostek + Crow + Peroneal + E.R.: COC 6.0	5/10	4.4	12.9	Ammonium chloride; calcium chloride; irradiated ergosterol	Died in two days
						5/11	8.3	5.9		
D. M.	7 weeks	+	+	++	Chvostek + Peroneal +	12/ 8	8.0	9.1	Calcium chloride; ultraviolet irradiation	Recovered in three days
						12/20	8.3	5.9		
A. M.	8	—	+	++++	Erb's sign: AOC 5.0; ACC 2.5; OCC 3.0; COC 6.0	4/ 7	4.0	4.4	Ammonium chloride; calcium chloride; ultraviolet irradiation	Died in nine days
						4/12	6.9	1.9		
						4/16	8.7	8.2		
J. R.	9	+	—	+++	Crow + Peroneal +	6/21	6.2	8.1	Calcium chloride; ultraviolet irradiation, cod liver oil	Improved in eight days
						6/28	6.5	4.9		
G. G.	8	—	+	—	Chvostek + E.R.: COC 4.0	3/ 5	5.5	7.6	Parathyroid extract; ultraviolet irradiation	Recovered in three days
						3/ 6	6.3			
						3/ 8	7.1			
F. D.	12½	—	+	+	Chvostek + Peroneal + Trousseau + E.R.: COC 1.0	3/ 8	4.9	7.5	Calcium chloride; ultraviolet irradiation; cod liver oil	Recovered in 19 days
G. P.	4	No history	No history	++++	Chvostek + Crow + Peroneal + Trousseau +	4/20	7.7	7.8	Ultraviolet irradiation; cod liver oil	Died in eight days
M. B.	8	—	+	++++	Chvostek + Crow +	8/22	7.7	7.4	Parathyroid extract; ultraviolet irradiation	Recovered in four days
						8/26	11.0			
						8/27	9.1			
B. M.	2 yr. 11 mo.	+	+	+++	Chvostek +	12/29	4.5	8.0	Parathyroid extract; calcium chloride; calcium bromide; cod liver oil; ultraviolet irradiation	Improved in one month
						12/30	6.3	7.0		
						12/31	8.5	4.9		
						1/ 2	8.6	5.3		
						1/ 4	7.2	4.1		
						1/10	7.0	4.6		
						1/21	8.8	5.5		
						1/25	9.5	5.5		

M. L.	11½	+	+	—	—	1/25	4.3	7.2	Cod liver oil; ultraviolet irradiation	Improved in twelve days
J. B.	5	No history	Cyanotic spells	—	10/30: ACC<AOC	10/29	5.6	8.6	Parathyroid extract;	Relieved on third day
					COC 7.0	10/31	7.3	9.1	ultraviolet	
					10/31: COC 6.0	11/ 1	9.6	7.9	irradiation;	
					11/2: COC 5.9	11/ 4	6.6		calcium chloride	
					11/4: COC 3.0	11/10	6.6	7.6		
					11/10: COC 3.0	11/18	8.4	7.1		
					11/27: COC 10.0+	11/19	12.8			
						11/27	9.3	7.4		
						12/ 2	10.8	7.7		
R. M.	5	—	+	++++	Chvostek +	3/16	5.8	...	Ultraviolet irradiation;	Cured in ten days
					Crow +	3/22	3.4		cod liver oil	
					Peroneal +	3/26	7.4	7.5		
					Trousseau +					
					E.R.: COC 3.0					
H. B.	2 years	—	+	++	Chvostek +	3/16	7.5	8.0	Cod liver oil; ultraviolet irradiation	Discharged in 2½ weeks; improved
					Crow +	3/19	...	5.4		
					Peroneal +					
P. G.	10	—	+	+	Chvostek +	5/19	5.4	...	Ultraviolet irradiation	Cured in three weeks
					Peroneal +	5/20	5.5	6.7		
					Trousseau +	5/26	7.1	7.6		
						6/ 2	8.9	8.0		
						6/ 9	11.4	8.6		
F. S.	4	+	+	++++	Crow +	2/ 1	7.2	12.0	No treatment	Died on fourth day
C. S.	5	—	+	+	Chvostek +	3/18	5.0	8.5	Cod liver oil	Discharged from hospital against advice
					Peroneal +	3/26	6.8	5.2		
					Trousseau +					
					3/17: COC 0.5					
					3/24: COC 2.0					
V. P.	5½	No history	—	+	Chvostek +	4/19	4.4	6.2	Ultraviolet irradiation;	Discharged on the ninth day; improved
					4/19: COC 5.0	4/21	5.0	7.2	cod liver oil; parathyroid extract	
						4/24	6.4	5.4		
						4/26	6.5	5.3		
R. H.	7	—	—	+++	Chvostek +	2/25	4.2	...	Cod liver oil	Cured in one month
					Peroneal +	3/ 7	6.6	6.1		
						3/20	8.3			
						3/26	9.3	7.6		
J. R.	7	—	+	+++	Chvostek +	4/ 9	6.0	5.5	Ammonium chloride;	Cured in sixteen days
					Peroneal +	4/13	7.4	7.8	ultraviolet irradiation	
						4/23	8.4	5.3	calcium lactate	

* E.R. indicates external resistance.

which the inorganic phosphorus was high. Scheer and Salomon [5] studied the calcium and inorganic phosphorus content of the serums in thirty cases of tetany and reported high phosphorus values in two of these cases. They noticed that in these two cases the condition was particularly severe and resistant to their usual therapy (administration of hydrochloric acid milk). Scott and Usher [6] analyzed the serums of twenty-one infants with tetany and found high phosphorus figures in two of the cases. In the course of his study on the use of ultraviolet light in the treatment of tetany, Hoag [7] analyzed the blood serum for calcium and inorganic phosphorus in nineteen cases, two of which showed values for phosphorus above the normal level. Powers [8] reported one case of severe tetany in a premature infant, aged 7 weeks, in whom the inorganic phosphorus content of the serum was 8.85 mg. per hundred cubic centimeters. The continued administration of calcium chloride for two weeks was unable, in this case, to prevent a recurrence of the convulsions and, at this time, the phosphorus was 10.8 mg. per hundred cubic centimeters. Tezner [9] examined the blood in nine cases of tetany and reported one in which the phosphorus content was 7.5 mg. per hundred cubic centimeters of serum. Table 1 gives a summary of the cases of tetany reported in the literature in which the inorganic phosphorus content of the serum was above the normal level.

At the suggestion of Dr. Schloss, we have reviewed the cases of infants with tetany admitted to the New York Nursery and Child's Hospital over a period of four and a half years. Elevated inorganic phosphorus values were encountered in twenty out of a total of eighty cases. The calcium of the serum was determined by Clark's modification of the Kramer-Tisdall method,[10] and the inorganic phosphorus by Tisdall's method.[11] The normal values for infants obtained by these

5. Scheer, K., and Salomon, A.: Zur Pathogenese und Therapie der Tetanie: I. Der Gehalt des Blutserums an saurelöslichen und lipoiden Phosphor, Jahrb. f. Kinderh. **103**:129, 1923.

6. Scott, John P., and Usher, Saul J.: Infantile Tetany, J. A. M. A. **87**: 1904 (Dec. 4) 1926.

7. Hoag, Lynne A.: The Treatment of Infantile Tetany with Ultraviolet Radiation, Am. J. Dis. Child. **26**:186 (Aug.) 1923.

8. Powers, Grover P.: Tetany as a Cause of Convulsions in Very Young Infants, J. A. M. A. **84**:1907 (June 20) 1925.

9. Tezner, O.: Trial of Strontium Salts in Infantile Tetany: Two Cases of Infantile Tetany Without Rickets, Monatschr. f. Kinderh. **35**:37, 1927.

10. Clark, E. P., and Collip, J. B.: A Study of the Tisdall Method for the Determination of Blood Calcium with a Suggested Modification, J. Biol. Chem. **63**:461, 1925.

11. Tisdall, F. F.: A Rapid Colorimetric Method for the Quantitative Determination of the Inorganic Phosphorus in Small Amounts of Serum, J. Biol. Chem. **50**:329, 1922.

methods are from 10 to 10.5 mg. per hundred cubic centimeters of serum for calcium from 5.5 to 6 mg. per hundred cubic centimeters of serum for inorganic phosphorus.

All the cases of tetany were analyzed with respect to etiology, symptomatology, complicating infections, mortality and blood chemistry. The etiology in the group with high phosphorus values differed in no way from that of the common form of tetany. Twenty-two per cent of the former and 28 per cent of the latter had not received cod liver oil. Clinical rickets was present in both groups.

The severity of clinical symptoms was as variable as those found in infantile tetany with normal or reduced inorganic phosphorus. The Chvostek, Trousseau and Erb signs were not always elicited, but the Chvostek reaction was positive in a large percentage of the cases. Con-

TABLE 3.—*Percentage Incidence of Accompanying Infections in Twenty Cases of Infantile Tetany with High Phosphorus Values and Sixty Cases of Ordinary Infantile Tetany*

	Severe		Moderate		Mild	
	Ordinary Tetany, per Cent	High Phosphorus Tetany, per Cent	Ordinary Tetany, per Cent	High Phosphorus Tetany, per Cent	Ordinary Tetany, per Cent	High Phosphorus Tetany, per Cent
Bronchopneumonia	13.3	20.0	6.7	....	3.3	....
Bronchitis	....	....	1.7	....	3.3	....
Upper respiratory infections						
Otitis media	8.3	10.0	8.3	....	13.3	25.0
Nasopharyngitis and tonsillitis	....	....	3.3	....	15.0	25.0
Diarrhea and dehydration	8.3	....	1.7	....	....	....
Very severe rickets	5.0	....	....	....	....	....
Other complications	3.3	10.0	11.7	15.0	28.3	

vulsions occurred in 72 per cent of the group with high phosphorus values and in 52 per cent of the infants with the usual form of tetany.

Twenty-six per cent of the cases of tetany with high phosphorus values and 18 per cent of the usual cases showed severe infections. Table 3 shows the percentage incidence of these infections in the two groups of cases. The infections were considered severe if the patient ran a protracted course with fever and marked prostration. The most severe infections were bronchopneumonia, infections of the upper respiratory tract with otitis media and gastro-intestinal intoxication with dehydration.

The mortality in the group with high phosphorus values was 20 per cent as compared with 22 per cent in the group with the usual form of tetany. In general, the mortality coincided with the severity of the accompanying infections.

The blood chemistry of the twenty cases with high phosphorus values may be seen in table 2. Two or more analyses of the blood serum for

inorganic phosphorus were made in thirteen patients. The majority of the infants had low calcium values. However, it is interesting to note that 3 or 15 per cent had a calcium content of the serum exceeding 7.5 mg. per hundred cubic centimeters prior to the institution of treatment. One had severe tetany with convulsions (D. M.) with a calcium of 8 mg. per hundred cubic centimeters of serum. Neither of the other two infants (G. P. and M. R.) in whom the calcium values exceeded 7.5 mg. per hundred cubic centimeters of serum had convulsions, but tetany was manifested in them by a positive Chvostek sign and laryngeal spasm. Of the thirteen published case reports in which the inorganic phosphorus content of the serum was above normal, three or 23 per cent had a calcium content exceeding 7.5 mg. per hundred cubic centimeters of serum (the two cases of Scheer and Salomon [5] and one case of Scott and Usher [6]).

The true significance of the inorganic phosphorus of the blood in the pathogenesis of infantile tetany is not yet known. It is generally accepted that tetany is caused by a decrease in calcium ions (Salvesen and Linder [12] and Drucker [13]). Kugelmass and Shohl [14] have shown that the calcium ion concentration in the blood is regulated by a system of buffers which are mixtures of weak acids and their salts which react to form insoluble calcium salts and soluble intermediate calcium salts. The most important of these buffers are the phosphate and carbonate ions. György [15] has attempted to modify the Rona-Takahashi formula for the ionization of calcium to show the repression exerted by the presence of increased phosphorus in the blood stream. He found low inorganic phosphorus values in most of the patients whom he examined, but he believed that these values are relatively increased over those present in the preexisting rickets. Hóllo [16] has criticized the validity of the extended Rona equilibrium. On the basis of mathematical and biologic studies, he has found it inapplicable to blood serum.

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12. Salvesen, H. A., and Linder, G. C.: The Relation Between Calcium and Protein of Serum in Tetany Due to Parathyroidectomy, J. Biol. Chem. **58**:635, 1923.

13. Drucker, Paul: Clinical Investigations Into the Pathogenesis of Infantile Tetany, Acta paediat., suppl. VI, 1927.

14. Kugelmass, I. N., and Shohl, A. T.: The Determination of the Equilibria Involving Calcium, Hydrogen, Carbonate, Bicarbonate and Primary, Secondary and Tertiary Phosphate Ions, J. Biol. Chem. **58**:649, 1923-1924. Kugelmass, I. N.: The Buffer Mechanism for the Calcion Concentration and the Determination of Calcion Buffer Values, J. Biol. Chem. **60**:237, 1924.

15. György, P.: Ueber den Gehalt des Blutserums an Kalk und anorganischem Phosphor im Säuglingsalter, Jahrb. f. Kinderh. **99**:1, 1922.

16. Hóllo, Julius: Zur Theorie der Calcium Ionisation in der Blutflüssigkeit, Biochem. Ztschr. **150**:496, 1924.

Dogs in which tetany was produced by parathyroidectomy showed an increase in the acid-soluble phosphorus in the blood (Greenwald [17]). Salvesen, Hastings and McIntosh [18] administered phosphate to parathyroidectomized dogs and noted that the calcium decreased as the inorganic phosphorus content of the serum rose and that when this occurred, symptoms of tetany became manifest.

SUMMARY

A series of eighty consecutive cases of infantile tetany occurring during a period of four and a half years has been reviewed. Twenty cases, or 25 per cent, showed an inorganic phosphorus exceeding 7 mg. per hundred cubic centimeters of serum. The significance of these high phosphorus values has been briefly discussed. No distinctive clinical characteristics were observed which might differentiate the group with high concentrations of serum phosphorus from those with normal or low inorganic phosphorus values.

161 West Sixty-First Street.

17. Greenwald, I.: On the Phosphorus Content of the Blood of Normal and Parathyroidectomized Dogs, J. Biol. Chem. **14**:369, 1913.

18. Salvesen, H. A.; Hastings, A. B., and McIntosh, J. F.: Blood Changes and Clinical Symptoms Following Oral Administration of Phosphates, J. Biol. Chem. **60**:311 and 327, 1924.

THE VALUE OF VACCINE IN THE PREVENTION OF WHOOPING COUGH *

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As whooping cough causes many more deaths than diphtheria, measles or scarlet fever,[1] it is important to know whether prophylactic injections of vaccine do or do not prevent the disease.

The use of convalescent serum to control and prevent whooping cough was reported as early as 1901, as quoted by Griffith and Mitchell,[2] and whooping cough vaccine has been in use for more than sixteen years. Fresh vaccine and stock vaccine have been used. While Huenekens [3] believed that stock vaccines some months old are valueless, Mishulov, Oldenbusch and Scholl [4] claimed that eight different stored preparations were tested at the end of four and one-half years and found to be highly potent, as measured by their power to stimulate specific antibodies in rabbits. Sauer and Hambrecht,[5] in their excellent study of the problem, stated that as a prophylactic measure vaccines are lauded more by the practicing physicians than by the pediatricians in medical schools or physicians in charge of institutions in which young children are housed. Smith [6] reviewed the literature appearing on this subject from 1919 to 1924. He stated: "The consensus of opinion would seem to suggest that the prophylactic use of vaccine may be expected to yield very satisfactory results, when used in sufficient dosage."

In 1921, Bloom [7] reported the prevention of an epidemic of whooping cough at an orphan asylum by means of injections of vaccine into those who had been exposed. A mixed vaccine was used, containing

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* From the Milwaukee County Home for Dependent Children.

* Read before the Central States Pediatric Society, Sept. 28, 1929.

1. Sauer, L. W., and Hambrecht, L.: Whooping Cough, J. A. M. A. **91**:1861 (Dec. 15) 1928.

2. Griffith and Mitchell: Diseases of Infants and Children, Philadelphia, W. B. Saunders Company, 1927, vol. 1, p. 557.

3. Huenekens, E. J.: Pertussis, Minnesota M. J. **10**:601 (Oct.) 1927.

4. Mishulov, L.; Oldenbusch, C. H., and Scholl, M.: Potency of Stored Pertussis Vaccines, J. Infect. Dis. **41**:169 (Aug.) 1927.

5. Sauer, L. W., and Hambrecht, L.: Whooping Cough, J. A. M. A. **91**: 1861 (Dec. 15) 1928.

6. Smith, L. W.: Review of Literature on Whooping Cough from 1919 to 1924, Am. J. Dis. Child. **28**:617 (Nov.) 1924.

7. Bloom, C. J.: Vaccine Therapy for Preventing Whooping Cough in Public Institutions, New Orleans M. & S. J. **73**:426 (April) 1921.

5,000,000,000 Bordet bacilli and 3,500,000,000 influenza bacilli. Three injections were given, ranging from 0.25 cc. for infants under 6 months to 1.25 cc. for children from 2 to 6 years of age. Bivins [8] claimed that pertussis vaccine is an effective agent in the prophylaxis of whooping cough. He cited a series of eighteen cases in which the patients were given prophylactic treatment after definite or expected exposure. He also used a mixed vaccine. After an interval of one year, some of the children had the disease in a mild form.

Friedlander,[9] Pellegrini,[10] Muñoyerro [11] and Fiano [12] also recommended the prophylactic use of vaccine. However, the reasons given for their faith do not seem convincing.

Undoubtedly, there are many instances in which prophylactic injections are given to children who have already had the disease. About 25 per cent of all cases of whooping cough occur in the first year of life, and the majority of cases occur before the sixth year, according to Griffith and Mitchell.[13]

If an exposed child does not develop whooping cough subsequent to the injection of vaccine, one must not conclude that the vaccine has immunized him. He may have had the disease previously, and in some cases he will contract it from a subsequent exposure. In like manner, an unvaccinated child may not contract it from other children in the family but may develop it during a later epidemic.

In 1921, the Council of Pharmacy and Chemistry of the American Medical Association had prepared, under its auspices, a series of articles dealing with serums and vaccines. In this it is stated [14] that immunization from whooping cough, by means of prophylactic injections is doubtful. At present, the physicians of Russia [15] are beginning to experiment with pertussis vaccine, while in Germany and Austria they are abandoning the use of it.

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8. Bivings, L.: Successful Vaccine Prophylaxis, J. M. A. Georgia **17**:484 (Nov.) 1928.

9. Friedlander, A., in Abt, J. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1925, vol. 6, p. 142.

10. Pellegrini, O.: Vaccine Therapy and Vaccine Prophylaxis of Whooping Cough, Pediatria **35**:71 (Jan. 15) 1927.

11. Muñoyerro, J. A. Alonso: Results of Preventive and Curative Vaccination in Whooping Cough, Arch. de med. cir. y espec. **24**:577 (Sept. 25) 1926.

12. Fiano, A.: Vaccination in Whooping Cough, Riv. di clin. pediat. **26**:685 (Sept.) 1928.

13. Griffith and Mitchell: Diseases of Infants and Children, Philadelphia, W. B. Saunders Company, 1927, vol. 1, p. 544.

14. Davison, W. C.: Pertussis Vaccine, J. A. M. A. **76**:242 (Jan. 22) 1921.

15. Zlatogorov, G.; Tets, E., and Gilman, L. A.: Prophylactic Inoculation Against Pertussis, Vrach. Gaz. Mosk. **32**:83, 1928.

In March of this year, Hoffman [16] reported unsatisfactory results with prophylactic injections. He used a mixed vaccine containing 4,000,000,000 Bordet bacilli, 500,000,000 Pfeiffer bacilli and 100,000,000 pneumococci per cubic centimeter. Abraham [17] reported the use of vaccine to protect a number of children who had been exposed, but 100 per cent of the vaccinated children contracted the disease. McLean [18] stated that conclusive evidence of the value of pertussis vaccine has not yet been obtained.

I shall present statistical records from the Milwaukee County Home for Dependent Children to show what effect, if any, the use of vaccine has had on the incidence of whooping cough.

The statistics of sixteen consecutive years were studied. During the first half of this period no vaccine was used, while during the second half of the period all children under 6 years of age received either pertussis vaccine or pertussis ecto-antigen, on entrance to the institution. Over 2,700 children received such prophylactic injections.

It was thought that a study extending over so long a period would more accurately reflect any influence that vaccine might have on the morbidity. Conclusions in regard to the efficacy of vaccine are too often arrived at without proper controls and without regard for the prevailing morbidity in the surrounding community at that time. It is manifestly unfair to compare the morbidity in a Children's Institution with that of the city of Milwaukee, where a large proportion are adults. Nevertheless, the whooping cough rate in the city from which the institution derives most of its children serves well in making a general comparison of the morbidity curves.

The mixed vaccine used contained 5,000,000,000 organisms per cubic centimeter, of which 4,000,000,000 were *Bacilli pertussis*. One cubic centimeter was given subcutaneously on alternative days for four doses. There was usually a rise in temperature of one or two degrees and considerable local reaction. These mixed vaccines were used from 1921 to 1926, inclusive.

During 1927 and 1928, the combined pertussis ecto-antigen was used. One cubic centimeter of this preparation is said to contain the antigens from 3,000,000,000 bacteria. This preparation was given intramuscularly daily for six doses. The first three injections were 0.5 cc., 1 cc. and 1.5 cc., respectively. The fourth, fifth and sixth injections consisted of 2 cc. each. As a rule there was very little or no reaction, but occasionally a scarletiniform rash appeared.

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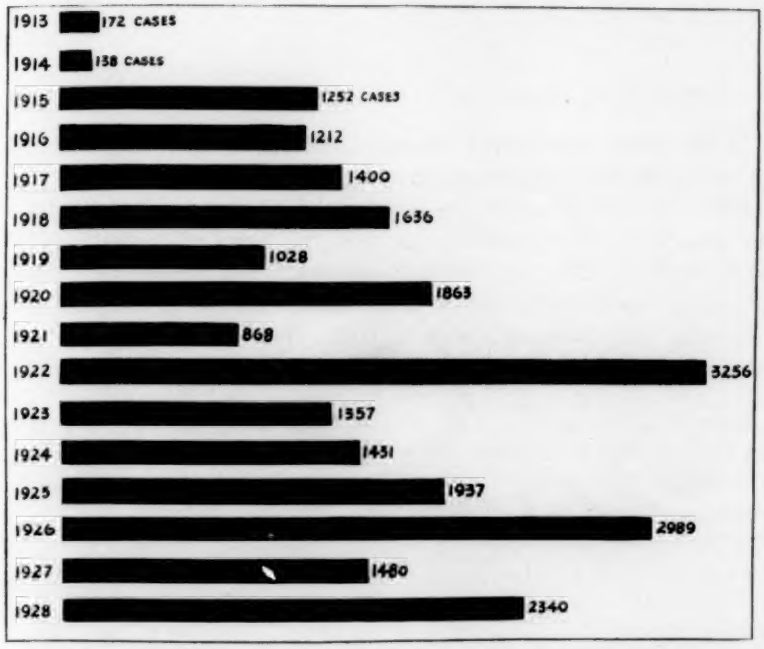

Fig. 1.—Cases of whooping cough in the city of Milwaukee from 1913 to 1928, inclusive.

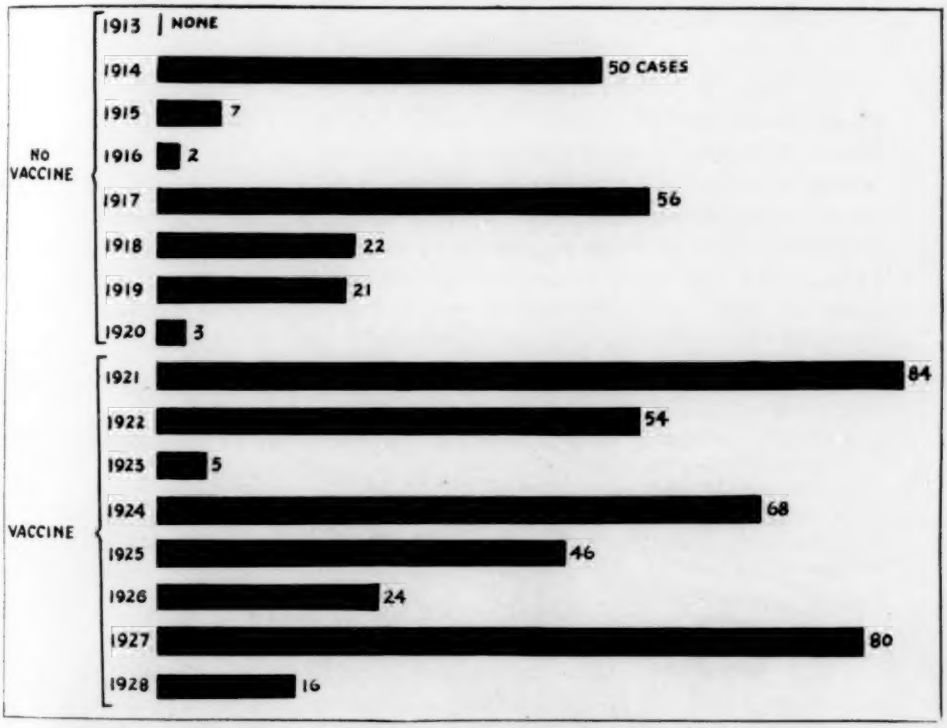

Fig. 2.—Prevalence of whooping cough at the Milwaukee County Home for Dependent Children from 1913 to 1928, inclusive. An eight year period during which no vaccine was used is compared with an eight year period during which it was used as a routine.

In the eight year period during which no vaccine was used, there was one year during which no cases of whooping cough developed, and another year during which the number of cases mounted to fifty-six. The total number of cases during the "no vaccine" period was 161, and the rate was 67.5 per thousand children. During this period, there were eight deaths that could be attributed to whooping cough.

During the "vaccine" period, 1921 to 1928, inclusive, cases of whooping cough ranged from 5 to 84 a year. The total number of

Incidence of Whooping Cough in the Milwaukee County Home for Dependent Children and in the City of Milwaukee from 1913 to 1928

	Milwaukee County Home for Dependent Children		City of Milwaukee	
	Whooping Cough Rate per 1,000 Children	Mortality of Whooping Cough Cases	Rate per 100,000 Population	Mortality of Whooping Cough Cases
No vaccine 1913 to 1920...	67.5	4.9%	255.5	2.8%
Vaccine used at Children's Home, 1921 to 1928 (inc.)	136.4	2.9%	384.7	0.8%

cases for these eight years was 377, and the rate was 136.4 cases per thousand children. During this period, there were eleven deaths due to whooping cough.

SUMMARY

As shown by the accompanying table and figures 1 and 2, the city of Milwaukee and the Milwaukee County Home for Dependent Children experienced a decided increase in the total number of cases of whooping cough and also in the morbidity rate during the past eight years. This increased morbidity occurred at the Home for Dependent Children in spite of routine prophylactic injections, but it is interesting to note that both the city and the institution had a lower whooping cough mortality from 1921 to 1928 than in the preceding eight years.

DIGITALIS STUDIES ON CHILDREN WITH HEART DISEASE

III. AURICULAR FIBRILLATION IN CHILDREN WITH AN EARLY TOXIC DIGITALIS MANIFESTATION *

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It is generally agreed that digitalis finds its greatest use and value in its slowing of the ventricular rate during established auricular fibrillation. That digitalis may, however, initiate and be responsible for the development of this arrhythmia in children with heart disease has been questioned on the ground that other factors responsible for the onset of this irregularity could not be ruled out.[1]

Since the rational use of digitalis depends in a great measure on a recognition and appreciation of its toxic manifestations, I have considered it worth while to call particular attention to the fact that digitalis in adequate doses can produce both the transient and the permanent forms of auricular fibrillation in children with heart disease. Moreover, the development of this arrhythmia is an early toxic manifestation during the course of digitalis therapy, and in some instances may result fatally. The close relationship of administration of digitalis and the onset of auricular fibrillation, independent of other factors, is shown by the following case reports.

REPORT OF CASES

CASE 1.—*Chronic rheumatic valvular heart disease, rheumatic fever; mitral stenosis and insufficiency, cardiac hypertrophy and dilatation; partial heart block, dropped beats, auricular fibrillation.*

History.—S. R., a boy, 6½ years of age, was admitted to the Montefiore Hospital on April 2, 1929. The family history was irrelevant. The boy was perfectly well until two years before admission (January, 1927), when he began to complain for the first time of pains in the joints of his legs. Both ankles were swollen, red and tender at that time. In February of that year, he was admitted to the New York Post-Graduate Hospital, where a diagnosis of heart disease was definitely established. For one and one-half years before admission, he had been in bed most of the time because of recurrent attacks of rheumatic fever, progressive loss in weight, increase in pallor and shortness of breath even at rest. For the two weeks before admission, he had had an intractable and unproductive cough.

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* Submitted for publication, Oct. 30, 1929.

* From the Medical Service of Dr. B. S. Oppenheimer, the Montefiore Hospital for Chronic Diseases.

1. Eggleston, C., in discussion of Schwartz, S. P., and Weiss, M. M.: Auricular Fibrillation in Children, Its Relationship to Rheumatic Heart Disease, Am. J. Dis. Child. **35**:534 (March) 1928.

Physical Examination.—On admission, physical examination revealed a pale, but well nourished boy sitting up in bed, not complaining of pain but breathing rapidly. The respirations were 40 and the heart rate was 140; the temperature was not elevated. There was moderate cyanosis of the lips and finger-nails. The superficial vessels of the neck were moderately distended, and there was marked pulsation in the suprasternal notch. The left nipple was retracted upward and outward toward the left. The anterior chest wall was deformed and protruding in the region of the second, third and fourth intercostal spaces. There was diffuse precordial pulsation extending from the levels of the third to the sixth intercostal spaces.

The apical impulse of the heart was in the sixth intercostal space in the posterior axillary line. Over that region there was a marked presystolic thrill. The first sound of the apex was replaced by a loud, blowing systolic murmur heard most clearly in the fifth intercostal space near the midclavicular line. A loud, blowing, diastolic murmur could be heard in the region of the second intercostal space to the left of the sternum and as far down as the xiphoid region. The heart rate was regular and varied from 110 to 140 beats per minute when counted over several minutes. The blood pressure in both arms was 110 systolic and 50 diastolic.

The base of the right lung posteriorly showed many moist râles. The abdomen was soft and lax. The liver was enlarged to 10 cm. below the right costal margin. There was shifting dulness in both flanks. The spleen was not palpable. The thighs, legs and feet were moderately swollen, and there was pitting on pressure.

Fluoroscopic examination of the heart revealed an enormous enlargement of the cardiac shadow. The left border of the heart was straight. The left auricle was dilated and encroached on the esophagus in the retrocardiac space. The secondary branches of the pulmonic artery were markedly enlarged.

An electrocardiogram taken on admission showed right ventricular predominance with notched P waves in all three leads and a P-R interval prolonged to 0.24 seconds.

A blood count taken at the same time revealed the presence of 24,600 white cells, 58 per cent of which were polymorphonuclears and 42 per cent lymphocytes. Examination of the urine did not show anything significant.

Course and Progress.—The boy's weight on admission was 45½ pounds (20.6 Kg.). His temperature varied from a minimum of 98.2 to a maximum of 103 F. On April 20, 1929, the temperature came down to a normal level and remained so for the ensuing ten days. Despite this, however, the boy's weight had increased during that time from 45½ pounds (20.6 Kg.) to 51 pounds (23 Kg.). On May 22, when his weight was 51¼ pounds (23.1 Kg.), examination disclosed marked signs of ascites with marked swelling of the lower extremities.

Despite the slight variations in the temperature and the presence of a regular sinus rhythm, in full knowledge that the boy was experiencing a recurrent bout of rheumatic fever, it was thought worth while to try a course of digitalis therapy. Accordingly, on May 22, he received 3 cc. of the tincture of digitalis. A similar amount was given to him daily thereafter. He was watched carefully for signs of nausea and vomiting and daily electrocardiograms were taken to note the variations in rhythm and to follow the changes in the P-R interval.

Within five days after the beginning of medication, the boy looked distinctly better. He had lost 7 pounds (3.2 Kg.) in weight. His ascites decreased and the edema of the lower extremities disappeared, but his respirations were still averaging 34, and his temperature was above normal. His heart rate was 124, and the unusual features observed at this time were the alternations of the pulse which became more evident from day to day.

In view of the marked improvement that had occurred in so short a time, digitalis was continued in the daily doses of 3 cc. However, on May 27, the temperature had again mounted steadily to 103.4 F., and the boy began to experience difficulty in breathing.

When seen at this time, he was sitting upright in bed and preferred to sleep in this position. His forehead was covered profusely with large beads of perspiration. His face was ghastly pale. Only alternate beats of the heart could be seen pulsating at the sixth intercostal space in the anterior axillary line. The alternation of the pulse was visible in the suprasternal notch. The heart sounds were loud. The first sound at the apex was of a booming quality. The lungs were clear. The edge of the liver, however, was down to the level of the umbilicus and was tender to palpation. There was again shifting dulness in the flanks, and a slight pitting on pressure over the tibia was becoming evident.

The question of further digitalis therapy was weighed carefully, and my associates and I considered that its further use was indicated in view of the fact that the boy had previously shown such an apparent improvement. He was given two more daily doses of 3 cc. of the tincture.

On May 30, the boy was distinctly worse. He vomited in the morning, and the regular alternation of the pulse gave way to a total irregularity of the heart with a pulse deficit of at least 24 beats per minute. With the onset of this irregularity, which proved to be that of auricular fibrillation, the respirations increased to 44. Large beads of perspiration appeared all over the body, which was cold to the touch. The bases of both lungs posteriorly were beginning to show the presence of moist bubbling râles. By noon of this day, the edge of the liver was palpable below the crest of the ilium. The systolic blood pressure had dropped to about 80 mm. of mercury. The boy was in a semistuporous state and hard to arouse.

He died on the evening of this day.

The electrocardiographic studies on this child, made during the administration of daily doses of 3 cc. of digitalis in the course of an active bout of rheumatic fever, are illuminating and deserve special attention.

Electrocardiograms.—On May 21, a control record revealed in addition to the right ventricular predominance, a widening and notching of the P waves in all three leads with a P-R interval which was slightly above the normal in that it measured 0.2 second. Part of the apparent prolongation was due to the bifid P wave. The T waves were upright in all three leads.

On May 23, the record followed the administration of 6 cc. of the tincture of digitalis and revealed a slightly longer P-R interval, the maximum measuring 0.24 second. The P-R interval was slightly variable from lead to lead. Lead 3 showed a straightening out of the S-T interval, and there was also a suggestion in this lead of electrocardiographic alternation, in that each alternate R wave was lower in height than the preceding wave. It will be recalled that clinical alternation was not observed until several days later.

On May 25, however, the electrocardiographic alternation was present in all three leads. It was most marked in lead 1, in which each alternate ventricular complex was notched and different in form, shape and size from the preceding one. The P-R interval was now 0.24 second. The S-T interval in lead 2 was straightened out; the T wave in this lead was now diminished in size, while T 3 was practically negative.

On May 27, the records followed the use of 18 cc. of digitalis. The electrocardiographic alternation persisted for four days. In the records obtained on this day, the Q R S complex in lead 1 had changed its form and was always notched.

5-21-29 Lead 1
Lead 2
Lead 3
5-23-29 Lead 1
Lead 2
Lead 3
5-25-29 Lead 1
Lead 2
Lead 3
5-27-29 Lead 1
Lead 2
Lead 3
5-28-29 Lead 1
Lead 2
Lead 3
5-30-29 Lead 1 Morning
Lead 2
Lead 3
5-30-29 Lead 1 Evening
Lead 2
Lead 3

whereas previously the notching was observed only in alternate beats. The P-R interval was 0.26 second. T 3 was markedly negative. Note that, with the increase in the P-R interval, the P lost its notching except in lead 3.

On May 28, the S-T interval of lead 2 was below the iso-electric line. The P-R interval had further increased to 0.34 second, and T 3 was markedly negative. The alternation was still visible, but in lead 3 only.

On May 29, the P-R interval was 0.28 second. The Q R S complexes resumed their normal shape.

On the morning of May 30, following the administration of 24 cc. of digitalis, the P-R interval showed variations from beat to beat measuring from 0.32 to 0.36 second. In the longer strips of lead 2 there was a progressive increase of the P-R interval from beat to beat with final failure of a ventricular response to a preceding auricular beat, resulting in "dropped beat" phenomenon.

During the afternoon of the same day, auricular fibrillation set in. The ventricular rate was slower with the auricles fibrillating than it was with normal sinus rhythm, indicating block in the A-V conduction system.

Comment.—To a child 6½ years old, with severe signs of heart failure, such as swelling of the legs and ascites, in the course of a recurrent bout of rheumatic fever, digitalis was administered in daily doses of 3 cc. for the purpose of producing diuresis and relieving ascites. Following the administration of 15 cc. of digitalis within five days, an apparent diuresis was produced, as evidenced by the loss of 7 pounds in weight (3.2 Kg.). Such encouraging results prompted the further use of digitalis in daily doses of 3 cc., even though the electrocardiograms showed signs of progressive increase in the P-R interval from day to day. Four days after the use of the drug was begun, alternation of the pulse developed. On this day, the electrocardiogram also revealed alternation.

The administration of 24 cc. of digitalis for eight days resulted in partial heart block with dropped beats, following which auricular fibrillation developed with a ventricular rate slower than the rate noted during the presence of sinus rhythm.

Death probably resulted from the complicating arrhythmias as a result of digitalis toxemia. It may be argued that since auricular fibrillation is observed occasionally as a terminal phenomenon in children with rheumatic fever and valvular heart disease, this might have been the case here. The progressive signs of digitalization, however, that are seen in the electrocardiograms from day to day, such as increase in the P-R interval and characteristic changes in the S-T interval and T waves, suggest that the fibrillation resulted from one and the same factor as the changes discussed, namely, excessive digitalis administration.

CASE 2.—*Chronic rheumatic valvular heart disease, rheumatic fever; mitral stenosis and insufficiency, aortic insufficiency, hydrothorax, cardiac arrhythmia, auricular fibrillation, bigeminal rhythm.*

History.—R. E., a girl, aged 12 years, was admitted to the Montefiore Hospital on Nov. 9, 1928. Her chief complaints were general malaise, shortness of breath and weakness. The family history was irrelevant. Chickenpox and measles were the only diseases mentioned in her past history. In February, 1927, it was noticed that the child was getting fidgety. It was impossible for her to keep still for any length of time. The left arm in particular was almost uncontrollable, and it was with difficulty that the girl could lift it up. She was taken to a psychiatrist at that time, who diagnosed the case as one of chorea. He also noted that the "heart was out of order" and advised the child to remain at home in bed for the next few months.

Within three months she recovered completely from chorea, and was well enough to attend school. Between April, 1928, and May of that year, no abnormal

movements were noted. At the end of May, the child began to complain of weakness, night sweats and fever. In the first week of June, she was admitted to the Mount Vernon Hospital, where for several weeks she was desperately sick with high fever and marked progressive secondary anemia. The anemia was severe enough to necessitate several transfusions. Between September and November, 1928, the date of her admission to the Montefiore Hospital, she remained in bed most of the time.

Physical Examination.—On admission to the hospital, the patient appeared to be a fairly well nourished and developed young girl, sitting up in bed. She showed marked pallor of the face, but there were no petechial spots anywhere. The superficial vessels of the neck were not distended. The left breast was swollen to about one and a half times the size of the right one. It was not tender or painful, and it did not pit on pressure. There was slight deformity of the chest in the region of the second, third and fourth left costosternal junctions. The apical impulse of the heart was in the sixth intercostal space in the anterior axillary line. A rough systolic thrill was felt over the fifth intercostal space in the anterior axillary line. The first sound at the apex was markedly accentuated and was preceded by a short presystolic murmur. A loud diastolic murmur could be heard over the entire chest. The pulmonic second sound was split and accentuated. The heart rate was 94 and regular. There was a slight sinus arrhythmia associated with respiration. The lungs were clear throughout. The abdomen was soft and lax, the edge of the liver being 4 cm. below the costal margin. The extremities showed no edema.

An electrocardiogram taken on admission showed a slight right ventricular predominance with sinus arrhythmia. The P waves were large in all 3 leads, and the P-R interval was within normal limits.

Fluoroscopic examination of the chest showed a moderate increase in the shadows of the hilus of the lung. The left ventricle was rounded and prominent. There was a slight dilatation of the pulmonary conus and pulmonic artery. The middle portion of the retrocardiac space was obliterated by an enlarged left auricle. The angle of bifurcation of the trachea was broadened, and the left main bronchus was displaced upward. The heart showed evidences of rotation, for the aorta was not visualized on the anterior film.

Examination of the urine did not reveal anything significant.

Course and Progress.—On Feb. 27, 1929, the child began to complain of cough for the first time since admission to the hospital. On this day her temperature was 101.4 F., the respirations were 32 and the heart rate was 124 and regular. Examination of the chest revealed some coarse vesicular breathing over both bases posteriorly. It was noted that within the two weeks prior to this examination, the patient had shown a rapid gain in weight. Whereas her previous weight had been 83 pounds (37.6 Kg.), it was now 93½ pounds (42.4 Kg.). On February 29, she showed the presence of shifting dulness in both flanks with signs of pretibial edema as well as edema of the feet.

In view of the rapid heart rate which now averaged 130 beats per minute, and because of the presence of signs of cardiac insufficiency, it was thought advisable to digitalize her. She was given 8 cc. of the tincture of digitalis on this day.

On March 1, the patient had a sudden chill with a further rise in temperature from the average of 102.3 to 105.2 F. It was observed that with the rise in fever her weight went down from 93½ pounds (42.4 Kg.) to 87⅜ pounds (39.6 Kg.) and that the signs of shifting dulness in the flanks had disappeared. As the reduction in weight and the marked diuresis were attributed to the digitalis, despite

the fact that her temperature was 104 F., she was given 8 cc. more of the tincture of digitalis on this day, so that she received a total of 16 cc. of the tincture in a period of five days. This caused no nausea or vomiting, and it was the consensus of the staff that the child was distinctly better.

On March 3, she experienced another chill, the temperature now rising to 105 F. in the morning and falling to a subnormal level toward evening. Examination on this day revealed the presence of dulness at the left base posteriorly. A blood count showed 21,000 white cells with 60 per cent polymorphonuclears and 40 per cent lymphocytes. The blood cultures were negative. It was believed that the child was having an exacerbation of rheumatic fever. Her weight was now 83¾ pounds (38 Kg.), so that within one week she had lost 10 pounds (4.5 Kg.) of fluid.

On March 7, as the loss of weight was attributed to the influence of digitalis, and as it was noted that the child was feeling well in spite of several chills, it was decided to give her more digitalis. She was given 8 cc. of the tincture. On the evening of this day, it was noted that, whereas previously the rate had averaged approximately 140 beats per minute, it now averaged only 84. On more careful clinical observation, the sequence of beats at the heart revealed the rhythm to be totally irregular, with a pulse deficit of about 14. Occasionally there was coupled rhythm. The electrocardiograms taken on this day showed auricular fibrillation with frequent alternate premature beats of the ventricles.

On March 8, the patient complained of slight visual disturbances. There was as yet no nausea or vomiting. She lay quietly in bed with her head resting on her arms. The temperature was 101 F.; her respirations were 28. The heart rate was slow, and there was bigeminal rhythm with auricular fibrillation. The premature beats persisted for several days, disappearing gradually. The child was conscious of the extra beats only when they occurred infrequently.

On March 13, six days after the discovery of auricular fibrillation with a slow ventricular rate, the electrocardiograms revealed sinus rhythm, but there were still evidences of digitalization from the diminished size of T 1 and negative T 2 and T 3. The temperature had now subsided, and within the next few days with its return to a normal level the weight curve began to show a rise again, so that on March 15 the patient weighed 91 pounds (41.3 Kg.).

Following the severe exacerbation of rheumatic fever and the disappearance of the cardiac irregularities, the child had an uneventful convalescence. Within three months (June 13, 1929) all signs of heart failure disappeared, the ascites abated, and she began to attend the hospital school. At that time of writing, she was ambulatory and feeling well.

Comment.—To a child with organic valvular heart disease and signs of recurrent exacerbations of rheumatic fever, because of an increase in weight due to cardiac insufficiency, digitalis was administered in large doses with the idea of lowering the heart rate and producing diuresis.

Following the administration of 32 cc. of the tincture of digitalis within nine days, the child developed auricular fibrillation with a slow ventricular rate but with a persistent coupled rhythm due to alternate premature beats of the ventricles. The fibrillation disappeared six days after its onset, and was replaced by a sinus rhythm with a rate of 140 beats per minute.

The heart rate was slower during the presence of auricular fibrillation than it was during sinus rhythm.

Although during the administration of the drug there was a definite reduction in weight amounting to over 10 pounds (4.5 Kg.), this cannot be definitely attributed to the drug, for in studying the natural history of chronic decompensa-

Fig. 2.—An electrocardiographic study of case 2, showing fibrillation with frequent alternate premature beats of the ventricles.

tion in children, it has been my experience frequently to see marked diuresis set in without the use of any drug in the presence of pyrexia. In one boy, the onset of rheumatic fever was responsible for the loss of over 15 pounds (6.8 Kg.) of weight in one day, 123 ounces (3.5 Kg.) of which passed out as urine.

The irregular beat of the heart began without warning, and it was thought at first that the slowing was a vagus phenomenon with a slight sinus arrhythmia. The coupled rhythm, however, and the electrocardiographic evidence left no doubt that the irregular beats were those of the gross arrhythmia of auricular fibrillation which, with the simultaneous appearance of ventricular premature beats, may well be attributed to excessive digitalis therapy.

Fortunately, this child recovered from her toxic manifestations of digitalis. The T waves of her electrocardiograms did not resume their normal size, shape and form until forty-two days after this episode.

SUMMARY

Attention has already been called, in a previous communication, to the possibility that digitalis may be one of the factors responsible for the development of paroxysmal auricular fibrillation in children with rheumatic heart disease. Two cases from the literature and an additional one were reported in which both clinical and graphic evidence confirmed the presence of the arrhythmia during the administration of the drug. In all three instances, normal rhythm of the heart beat was present before the digitalis was administered and after the disappearance of these irregularities.[2]

In this paper, two more cases are added, one of a paroxysmal type and one terminal in character.

In one child, the combined presence of alternate premature beats of the ventricles in association with a slow ventricular rate during auricular fibrillation leaves no doubt that digitalis was in a great measure responsible for initiating both irregularities; for coupled rhythm during auricular fibrillation is an almost invariable toxic digitalis manifestation.

Of greater significance are the clinical course and the electrocardiographic observations of the child in whom terminal auricular fibrillation developed as a result of constant digitalis administration. In this boy the daily addition of 3 cc. of the drug produced a progressive increase of the P-R interval from day to day, leading finally to partial heart block with dropped beats and ending with auricular fibrillation. The presence of other electrocardiographic evidences of digitalization, such as block, and marked negativity of the T waves in his records suggest that the fibrillation although terminal in character was due to the excessive use of the drug and not solely to rheumatic fever.

The question arises as to whether in this child the auricular fibrillation that developed during the use of digitalis might not have been initi-

Fig. 2.—An electrocardiographic study of case 2, showing fibrillation with frequent alternate premature beats of the ventricles.

2. Schwartz, S. P., and Weiss, M. M.: Auricular Fibrillation in Children, Am. J. Dis. Child. **36**:22 (July) 1928.

ated by the same factor that led to the development of progressive block, namely, vagal stimulation.[3]

There is both experimental and clinical proof that in certain instances vagal stimulation may initiate auricular fibrillation. This subject has been adequately summarized recently by Resnick,[4] who was able to induce a transient type of auricular fibrillation in seven patients with marked myocardial damage by the administration of effective doses of a potent preparation of digitalis. In one of his patients, sinus rhythm was restored following the injection of atropine sulphate.

Resnick, however, justly concludes that since atropine could not restore sinus rhythm in all his patients, an additional factor besides vagal stimulation was necessary for the initiation of auricular fibrillation, namely, marked myocardial insufficiency.

It is probable that this was the case in the children whose cases are reported here, since both were in the active stages of rheumatic fever with advanced signs of cardiac failure.

That auricular fibrillation is an early disturbance of the cardiac mechanism which digitalis in effective doses may cause in children can be further appreciated from the fact that this arrhythmia has been invariably noted in children before the onset of premature ventricular beats.

For example, in a series of fifty consecutive cases of children with sinus rhythm and far advanced organic valvular heart lesions to whom effective doses of digitalis were administered during the course of cardiac insufficiency at the Montefiore Hospital, none showed the presence of premature beats of the ventricle as an early manifestation of excessive digitalization.

On the other hand, premature beats of the ventricles were observed, either singly or in groups, in 80 per cent of twenty children with rheumatic heart disease after auricular fibrillation was established.

Moreover, in all of the children whom my associates and I have studied in whom auricular fibrillation developed during the administration of digitalis, the premature beats of the ventricle appeared after its establishment. Since, experimentally, premature beats of the ventricles

3. It has been shown previously that it is possible temporarily to eliminate digitalis block in children by the subcutaneous administration of an adequate dose of atropine sulphate, thereby proving that the various early forms of depression of conduction in children following digitalis are vagal in origin. Schwartz, S. P., and Schwedel, J. B.: Digitalis Studies on Children with Heart Disease: II. The Effects of Digitalis on the Sinus Rate of Children with Rheumatic Fever and Chronic Valvular Heart Disease, Am. J. Dis. Child. **39**:298 (Feb.) 1930.

4. Resnick, W. H.: Transient Auricular Fibrillation Following Digitalis Therapy with Observations Upon the Reaction of Atropine, J. Clin. Investigation **1**:181, 1924.

as a result of digitalis administration represent the first direct action of the drug on the heart muscle, it is fair to assume that auricular fibrillation, which comes earlier, falls into the first stage of digitalis action suggested by Cushny, namely, excessive vagal inhibition. Further studies in adults with rheumatic heart disease support this contention.

SUMMARY

Two children are reported to whom digitalis was administered during an active bout of rheumatic fever because of several signs of heart failure, such as enlargement of the liver and swelling of the face with ascites.

In one child, aged 6½ years, the daily administration of 3 cc. of the tincture of digitalis resulted in a progressive increase of the P-R interval with dropped beats and the development of auricular fibrillation after a total of 24 cc. of the drug had been given within eight days. Nausea and vomiting did not appear until the development of the fibrillation. Death resulted seven hours after the establishment of the arrhythmia. In another child, aged 8½ years, auricular fibrillation, with a slow ventricular rate and alternate premature beats of the ventricles, developed after 32 cc. of the tincture had been administered within nine days. The fibrillation appeared before the premature ventricular beats and disappeared within six days.

In both instances, the development of the fibrillation was considered the result of vagal stimulation by the drug during a period of active carditis.

Because of the dangers involved in the administration of digitalis during active carditis, it is concluded that digitalis is contraindicated in such children with rheumatic fever and signs of cardiac insufficiency.

TETANUS NEONATORUM

REPORT OF A CASE WITH RECOVERY *

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Tetanus neonatorum has in past years been given a diversity of names, having been known as the "scourge of St. Kilda," "seven day sickness," "nine day fits," "trismus," "trismus nascentium" and other names of uncertain significance. For many years this disease was a "will-o-the-wisp" for the medical profession, puzzling many of the great scientists. Even to the present day, the pathology and treatment remain in the realms of the uncertain.

It is a common belief that the disease is a great rarity. Johnston, in 1928, began his case report by saying, "Tetanus Neonatorum must be an extremely rare disease today." Statistical investigation, however, shows that tetanus neonatorum yet flourishes in some parts of the world, including the United States.

The statistical data in this study were obtained from individual correspondence with each State Bureau of Vital Statistics and through the U. S. Bureau of Census. The assimilation of these data was difficult, chiefly due to the fact that tetanus neonatorum is not listed in the International List of Causes of Death, but is included under the general head of tetanus. Replies were received from thirty-nine of the forty-eight states to which inquiries were made. Only eleven states had a separate classification for tetanus neonatorum. A report of the cases of tetanus in patients less than 1 month of age was sent from three other states. A total of 2,110 cases was reported from these fourteen states. The distribution of these cases may be seen in table 1.

Anders and Morgan, in 1906, published the results of a detailed statistical study of tetanus neonatorum from 1850 to 1906. I have continued this study from 1906 to 1929. Anders and Morgan, through the United States Census and other sources, reported the total number of deaths recorded from 1870 to 1900 as 4,788. That this disease is taking as great a toll in the twentieth century as in the late nineteenth century is forcefully shown in the data given in table 2, which were compiled from the United States Census Reports.

An unbelievable total of 5,767 deaths from tetanus in patients less than 1 month of age was reported from 1910 to 1927. It is true that there has been a considerable decrease in the incidence of the disease in recent years, but despite that fact, the results in table 2 are a striking proof that tetanus neonatorum is not a rare or obscure disease.

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From a rather exhaustive review of the English medical literature for the past hundred years, I was impressed with the lack of consideration this fairly frequent and highly fatal condition has received. The reports of only a few cases and an occasional article covering the disease as a whole could be found. The work which has been done adds little to the knowledge of the disease. A quotation from Mackintosh's

TABLE 1.—*Distribution of Cases of Tetanus Neonatorum in the United States*

State	Years	Deaths	State	Years	Deaths
Alabama	1922–1929	105	District of Columbia	1905–1920	44
Louisiana	1922–1929	407	Pennsylvania	1910–1928	247
North Carolina	1906–1929	818	Minnesota	1916–1929	31
South Carolina	1916–1929	264	Wisconsin	1924–1928	8
Ohio	1910–1920	84	Delaware	1920–1927	5
Massachusetts	1916–1928	44	Kansas	1924–1929	17
California	1922–1928	34	New Hampshire	1922–1929	2
			Total		2,110

TABLE 2.—*Data for Cases Occurring from 1906 to 1927*

Year	Deaths Under 1 Year	Deaths Under 1 Month	Per Cent of Population Registered
1927	238	215	91.3
1926	239	211	89.8
1925	238	218	89.4
1924	319	290	88.5
1923	364	328	87.6
1922	356	325	85.3
1921	385	354	82.2
1920	372	343	82.2
1919	393	360	81.1
1918	351	336	78.5
1917	329	304	73.4
1916	332	309	70.8
1915	299	280	67.5
1914	368	352	67.2
1913	360	351	65.5
1912	413	393	63.5
1911	398	378	63.2
1910	427	411	58.3
1909	422		
1908	284		
1907	509		
1906	520		
Total	7,925	5,767	

"Practice," published in 1834, gives a fairly accurate account of the disease as it is known today:

It is a disease seldom seen in this country, and is more particularly an affection of the negro children of warm climates; attacking them between the seventh and fifteenth day after birth. Neither preceded nor accompanied by any febrile movement. The disease steals on in the following manner: Children lose flesh and strength, are affected with drowsiness and frequent yawning; they suck with increasing difficulty and at last are either unable to suck the breast or to swallow: the skin gradually puts on a yellow appearance and by and by the jaw is observed to become stiff and the muscles rigid. General convulsions precede death which happens within two or three days after the attack. . . .

The true pathology of the affection baffles all inquirers. . . . No treatment appears to have much effect after the disease is once established. . . .

No attempt has been made, so far as I could ascertain, within the past fifty years to assimilate the knowledge of this disease and to draw some useful conclusions. There has never been an analysis of a series of cases with recovery. It is for that purpose that this study is presented. I have taken twenty-seven cases with recovery, the results of which are shown in table 5, and twenty-seven cases with death, the

TABLE 3.—*Cases with Death*

Number	Onset	Duration	Temperature	Umbilical Cord	Treatment
1	7	5	103	Healthy	Tetanus antitoxin, 25,000 units
2	7	1	106	Infected	None
3	5	3	101	Infected	Tetanus antitoxin, 2,000 units; bromides
4	3	3	103	Infected	Tetanus antitoxins, 2,500 units
5	7	?	104	Infected	Tetanus antitoxin, 10,000 units; magnesium sulphate
6	10	5	103	Healthy	Tetanus antitoxin, 40,000 units; chloral hydrate and bromide
7	6	3	103	Infected	Tetanus antitoxin, 20,000 units
8	?	?	102	Infected	Tetanus antitoxin, 2,500 units
9	5	5	104	Infected	Tetanus antitoxin, 14,000 units
10	4	4	103	Infected	Tetanus antitoxin, 3,000 units
11	7	1	?	Infected	Tetanus antitoxin, 1,500 units
12	10	2	?	Healthy	Magnesium sulphate; chloral hydrate
13	7	7	?	?	?
14	6	5	104	Infected	Tetanus antitoxin, 15,000 units
15	7	3	?	Infected	Tetanus antitoxin, 10,00 units

TABLE 4.—*Number of Cases with Death Reported in the Literature*

Number	Onset	Duration	Temperature	Umbilical Cord	Treatment
1	8	5	99-106	?	None
2	10	13	?	Healthy	Tetanus antitoxin, seventh day
3	8	10	?	Healthy	Tetanus antitoxin
4	?	12	105	Infected	None
5	8	5	?	Infected	None
6	7	4	104	Infected	Tetanus antitoxin, chloral hydrate and bromide
7	7	3	97-104	Infected	Tetanus antitoxin, chloral hydrate and bromide
8	12	13	97-107	Infected	Chloral hydrate and calabar bean
9	4	5	?	Healthy	None
10	6	3	?	Infected	None
11	7	5	?	Infected	Chloral hydrate
12	4	2	?	Healthy	Chloral hydrate

data for which are shown in tables 3 and 4. The cases in table 3 are from the records of the Roper Hospital, Charleston, S. C. Included in this study is one hitherto unreported case in which the patient recovered. I have also had the fortune to assist in the treatment of a patient who recovered at the Infants and Childrens Sanatorium at Saluda, N. C., in 1927, and also to observe one case with death at the Roper Hospital in September, 1927. Several of the cases reported in the literature were found to be of doubtful nature and were rejected.

ETIOLOGY

The etiology of tetanus neonatorum has not as yet been proved beyond doubt. The similarity of the symptoms to those of traumatic tetanus has led to the association of the two, and it is generally conceded that they are produced by the same organism. Indeed, this view is supported by the finding of the tetanus bacillus by Kitasato in a case of tetanus neonatorum and by the demonstration of the organism in two of the cases reviewed in this study. In the series of cases presented here, the apparent inefficiency of the tetanus antitoxin in the treatment for this type of tetanus as compared to traumatic tetanus seems to throw some little doubt on the etiology. It is evident that not in a single case in this series can it be definitely stated that the tetanus antitoxin was the cause of recovery.

Moschion and Levret, during the first century, A. D., hinted that stagnation of the blood in the unbilical vessels caused trismus in infants. M. Bartram of South Carolina must be credited with first definitely calling attention to the part the cord played in the early stages of this disease. In the "Transactions of the College of Physicians," 1793, he wrote as follows: "For the most part it (trismus nascentium) makes its attack with the dropping of the cord, though rarely it occurs several days after it has entirely healed. This is not surprising when it is compared with several incidences upon record of tetanus in adults taking place after the wound is cicatrized." He also must have had in mind some relation between this condition and traumatic tetanus of adults.

Until the discovery of the tetanus bacillus by Nicolaier, in 1885, many and numerous causes were ascribed to the elusive "trismus." Almost every conceivable theory was advanced that might be prompted by superficial observation under any circumstances. For a long time exposure to adverse weather conditions was accepted as the cause. "The abuse of spiritous liquors" and "irritative impressions made on the nervous system by compression of the cord in tying it" were advanced as possible explanations. Underwood remarked with all seriousness in an article on the subject years ago, as follows: "The cause has at last been clearly ascertained and happily its prevention by Dr. James Clark, who perceiving that those houses were free of the disease in which there were no fires, very soon demonstrated it to be owing to the smoke and burning wood; the negro houses having no chimney to carry it off." In an epidemic on the Island of St. Kilda, the cause was attributed to the "frequent intermarriages on the island," "the oily nature of the food," "mismanagement of the cord," etc. One shrewd observer philosophized: "It is a wise provision of Providence for preventing a redundant population on a rock where food is limited," and well may it be said that perhaps he was not so far from the fundamental reason for all disease.

The illustrious Marion Sims, during the early years of his scientific investigation, propounded a theory of the pathogenesis of "trismis nascentium" which immediately drew the attention of the medical profession of the whole country. Sims' investigations and theories were the means of arousing a general interest in this dread slayer of the new-born. In an article published in 1846, Dr. Sims, with a small series of cases, attempted to establish that trismus nascentium was due to the mechanical pressure exerted on the medulla and its nerves by the inward displacement of the occiput bone, this condition resulting from the infant being placed on its back with the head resting on some hard substance and kept in this position constantly during the first few days of life. He presented six cases which seemed to bear out his contention and, remarkable, to say the least, one of the patients on being placed on its side made a rapid recovery. In closing his article, he wrote, "If I am wrong, contemporaneous observers will prove it; if I am right, future generations will feel it." He lived to see his theories altered and finally destroyed by accumulating facts.

Without doubt, the point of entry is in practically every case the umbilicus. Only in one case in this series was the point of entry definitely other than the cord. This case resulted from an improperly performed circumcision. In only nine cases of fifty-four was the stump of the cord stated as being healthy. In five of these nine the onset was given at eight days or beyond from which it might be assumed that the cord had had time to heal. For one of the remaining four, no history was given as to the date of onset. It is no wonder that with the rude state of obstetrics in some localities, even at present, this fatal disease should frequently occur. Dr. Longer, as late as 1916, described as follows the usual procedure of a labor case in China:

> The usual preparation for lying-in by a poor Chinese woman of the Hunan Province consists of getting together a roll of the cheapest paper made of straw, a large washtub, a small wooden stool, two shovelsful of wood ashes wrapped in the straw paper for the bed, an old pair of scissors and a string.
>
> The mother sits on the edge of the stool, leaning against a friend or a washstand, the child is born into the tub which already holds the amniotic fluid and previous discharges; and is caught up by a midwife or a neighbor. The cord is tied by any old string; and the child rolled into the oldest, dirtiest garment the household affords. With such ushering into life, it is small wonder that in our woman's dispensary there are frequent cases of tetanus neonatorum. The person who brings the child generally tells us that the baby won't nurse. One finds the muscles convulsed, the umbilicus either red or angry looking or quite black and foul smelling. The child is almost invariably 10 days old. . . . Of late we have not tried to help them in any way as it always was hopeless.

Following an investigation of the terrific epidemic on the Island of St. Kilda, Professor Reid, in 1890, instructed and helped to carry out a proper treatment for the umbilical stump, which included the applica-

tion of an efficient antiseptic. The results were remarkable, greatly reducing the incidence of this disease on the island. The present method of treating the cord of the new-born has done much to stamp out tetanus and other diseases resulting from an infection of the cord.

History presents many striking incidences of the communicable nature of the disease. Arthur Mitchell wrote in the *Edinburgh Medical Journal* that of 125 children the offspring of 14 couples residing on the Island of St. Kilda before 1860, no less than 95 died within the first fourteen days of life from trismus. In the Rotunda Hospital, Dublin, in 1772, of every 6 infants born, 1 died of this disease. Seventy-five years ago, the attention of the medial profession was directed to the prevalence of tetanus on the Island of Heimancy off the coast of Iceland. Here scarcely a single infant lived beyond the age of 2 weeks, all dying from the ravages of the fatal tetanus. On the mainland, however, practically no cases occurred.

PATHOLOGY

The true pathology is undetermined, even if it is assumed that it is the result of infection by the tetanus bacillus. No extensive investigation of the pathology of tetanus neonatorum has been attempted within the past fifty years. In the cases presented here, necropsies were performed in a few, and the results of those are inconclusive.

Hartigan, in 1884, presented a paper summarizing the results of 150 autopsies which he performed in the city of Washington in five years on cases of tetanus neonatorum. All were apparently typical cases. These autopsies consistently showed extravasation of blood and blood-tinged serum into the spaces around the spinal cord and cerebellum with infection generally of all the meninges.

Dr. Finckel, in Hecker's "Annalen," in 1834, recorded observations on autopsies on twenty cases, finding an "effusion of blood" around the spinal cord between the bony wall and dura in sixteen. All but one showed extravasation of blood over the surface of the brain. Meningeal inflammation was present in nine.

It is likely in most cases of tetanus neonatorum that extravasation of blood and injection of the meninges will be present, but this is probably the result of the spasms and of the cardiac and respiratory embarrassment. All that can be said definitely about the pathology is that there is a severe toxemia which seems to have an especial affinity for the nervous system.

Tetanus neonatorum is one of the most fatal of all diseases. Shaw and LaFetra, in their system of books on the "Diseases of Children," took an unwarranted optimistic view of the mortality in this disease, stating that from 20 to 30 per cent of the patients recover. Holt gave the mortality as between 95 and 98 per cent, as does Abt in his system

of pediatrics. Holt stated that he had personally seen only one case in which the patient recovered. In a carefully compiled report of thirty-one cases occurring in Minnesota from 1916 to 1928, all were fatal; of thirty-four cases in California from 1922 to 1929, thirty-one were fatal. The fact that in an extensive review of the English literature on the subject, only twenty-seven cases with recovery could be produced is an indication of the exceedingly unfavorable prognosis.

Fig. 1.—Infant with tetanus neonatorum in the midst of a tetanic spasm. Note the opisthotonos, the adduction of the knees and the typical facial expression.

Fig. 2.—Same patient as shown in figure 1 relaxed between spasms. Note the facial expression and the typical clenched fist. The nasal tube is in place for feeding.

DIAGNOSIS

Any one who is familiar with the symptoms of traumatic tetanus would hardly fail to make a diagnosis. If careful attention is given to the taking of the history, it often will be found that for perhaps a day before the baby refused to nurse, the mother noticed that the baby would start from its sleep and would moan languidly or give vent to a sharp cry as if in pain. Sometimes there will be restlessness and twitching of the upper extremities or other premonitory signs of pending nervous distress. Usually little attention is paid to these symptoms by the mother. In most cases, the first symptom presented to the physician

is inability of the infant to nurse. In the series of cases here analyzed, this symptom was not lacking in a single case. Following this there is noticed a definite stiffening of the jaws which resists opening even by force. At this time the infant may develop a little fever, or perhaps this does not occur until a day or two later. Fever was present in every case in the series in which the temperature was recorded, the temperature more often rising to 104 and sometimes to 106 F. Some writers attribute the fever to the effect of the tetanus antitoxin, but in these cases all had fever alike whether they received the antitoxin or had no treatment. The chief symptom strikes with the swiftness and ferocity of a bolt of lightning. The infant suddenly passes into a terrific clonic spasm, every muscle contracting with violent force. The neck is rigid and the face muscles are drawn into a typical "risus sardonicus." The abdomen is boardlike, the knees are adducted, the thumb is grasped by the other fingers and the hand is turned inward. The patient may attempt to cry, but this is prevented by spasmodic contraction of the glottis which produces instead a peculiar "croak." The clonic spasm becomes tonic, and after several seconds or perhaps minutes, it passes off. The infant relaxes and is thrown into another convulsion by a breath of wind, a vagrant fly or perhaps the slamming of a door. In those cases in which the infant survives the first few hours, a typical opisthotonos transforms the patient into a semicircle. The muscles are in a constant state of hypertonus, convulsions occurring at frequent intervals. Feeding becomes increasingly difficult, and in some cases the patient dies of lack of nutrition and body fluids.

A point in diagnosis which has received little attention, and which cannot be found in any textbook on pediatrics, is the similarity of symptoms in some cases of cerebrospinal infection resulting from the so-called "sepsis neonatorum" to those of tetanus.

Cameron called attention to "sepsis neonatorum" in which there is an infection of the cerebrospinal system of streptococcal and occasionally meningococcic origin, giving most of the typical symptoms of tetanus neonatorum. He quoted the history of five patients which seemed to bear out this contention, four of whom recovered.

TREATMENT

The treatment of new-born infants with tetanus has so far been ineffective. The passing of time and the discovery of tetanus antitoxin have done little to decrease the fatality of this disease. It seems to me that the most that can be done with the present treatment is to attempt to control the irritability and spasmodic contraction of the infant and perhaps prolong its life for a few days; also, unfortunately, its suffering. In this regard, it is interesting to compare an analysis by Smith of cases resulting in death in his "Diseases of Children," published in 1870,

before the use of tetanus antitoxin and large doses of antispasmodics, with the series of cases resulting in death here presented, all of which occurred since 1870.

SMITH'S SERIES (31 cases)	MY SERIES (26 cases)
1 lived three hours	2 lived one day or less
11 one day or less	3 two days or less
12 two days or less	6 three days
4 three days	11 four to eight days
3 four days	4 eight to fourteen days

SMITH'S SERIES: 77 per cent died within forty-eight hours, only 9 per cent lived four days or more.

MY SERIES: 15 per cent died within forty-eight hours, 58 per cent lived four days or more.

Occasionally a patient recovers. The cure in these cases has been attributed to a great variety of different drugs and mechanical procedures. Among these one finds mainly the antispasmodics, such as eserine sulphate, curare, chloral hydrate, U.S.P., the bromides and more recently magnesium sulphate. Following Sims' work previously referred to, several cases were reported in which the patients were cured by being placed on the side, and in some instances operations were devised for lifting the occipital bone out of its supposedly disastrous position beneath the parietal bones. None of these proved successful.

It has been said by some writers and pediatricians that if tetanus antitoxin were given during the first day or sooner, the infant might be saved. This contention is not borne out, however, in this series of cases. Of the twenty-seven cases with death, five of the patients received the tetanus antitoxin within the first twenty-four hours, one of them receiving 20,000 units, the others from 1,500 to 10,000 units; seven received the antitoxin within forty-eight hours or less. One received 5,000 units intraspinally and 40,000 units intramuscularly; the others received from 10,000 to 20,000 units intramuscularly. It will be noted that the doses were sufficiently large. Of the twenty-seven patients who recovered, fifteen received no antitoxin. In one case the patient was not treated until the eighteenth day. In the other cases the antitoxin was given several days after the onset in most instances.

According to some observers, the use of magnesium sulphate offers the best results. In an article in the AMERICAN JOURNAL OF DISEASES OF CHILDREN, September, 1926, Muelchi recommended the use of magnesium sulphate. She quoted that Bratusch Marrain at the Kinderklinik at Gratz reported that from 1906 to 1921 without the use of magnesium sulphate, the mortality was 97 per cent in twenty-eight cases of tetanus neonatorum. From 1921 to 1923, eight patients were treated with recovery in four. Muelchi included a case of her own with recovery

which she attributed to the use of magnesium sulphate. The patients seen by me seem to have been helped by frequent injections of 50 per cent magnesium sulphate in doses of from 10 to 15 minims (0.6 to 0.9 cc.).

Prompt energetic treatment to control the convulsions is indicated if the patient is to have a chance to recover. Magnesium sulphate, from 15 to 20 minims (0.9 to 1.2 cc.) of a 50 per cent solution, should be given subcutaneously at once. The usual precaution of having calcium chloride solution easily available should be observed. Tetanus antitoxin should be administered, from 2,000 to 5,000 units intra-

TABLE 5.—*Cases in Which Patients Recovered*

Number	Onset	Duration	Maximum Temperature	Umbilical Cord	Treatment
1	?	?	104	Infected	Tetanus antitoxin, chloral hydrate and bromide
2	9	16	100	Infected	Antitetanus serum
3	5	22	?	Infected	Chloral hydrate
4	9	35	108	Infected	Antitetanic serum
5	10	20	?	Infected	Tetanus antitoxin
6	14	?	?	Infected	Tetanus antitoxin
7	6	?	?	?	Eserine, chloral hydrate and bromide
8	3	?	104	?	Tetanus antitoxin, chloral hydrate and bromide
9	9	?	?	?	Tetanus antitoxin
10	6	6	104	?	Tetanus antitoxin
11	6	20	103	?	Chloral hydrate
12	8	6	101	Infected	Tetanus antitoxin, chloral hydrate and bromide
13	10	34	103	?	Tetanus antitoxin and magnesium sulphate
14	10	?	103	Infected	Tetanus antitoxin, chloral hydrate and bromide
15	5	20	104	Healthy	Chloral hydrate and bromide
16	5	28	106	Infected	Tetanus antitoxin, chloral hydrate, bromide and magnesium sulphate
17	9	20	?	Infected	Chloral hydrate
18	9	?	?	Infected	Aconite and bromide
19	6	20	104	Infected	Tetanus antitoxin, chloral hydrate, bromide and magnesium sulphate
20	7	?	?	Infected	Chloroform stupe to spine
21	7	20	?	Infected	Chloroform stupe to spine
22 23	?	?	?	?	Cannabis indica
24	?	?	?	?	"Laying patient on side"
25	?	?	?	?	"Laying patient on side"
26	?	?	?	?	None
27	13	21	100	Infected	Chloral hydrate and bromide

spinally and 10,000 to 20,000 units intramuscularly. The magnesium sulphate should be repeated in doses of from 10 to 15 minims (0.6 to 0.9 cc.) three or four times in twenty-four hours to control the convulsions. Chloral hydrate from 3 to 5 grains (0.195 to 0.324 Gm.) with calcium bromide from 5 to 8 grains (0.324 to 0.52 Gm.) in 2 ounces of water should be administered by rectum every four hours. The patient should be kept in a dark, quiet room, being disturbed only to feed and to give medication. The chloral hydrate and bromide may be given in suitable doses with the milk in those cases in which there is no vomiting.

The greatest exigency will be encountered in the feeding of the infant, nasal and oral gavage having to be resorted to in most cases.

Speed and precision are prime requisites, as a fraction of a minute wasted may cost the life of the infant by asphyxiation. The food should be given in concentrated form and at less frequent intervals during the first few days so as to limit the handling of the patient as much as possible. The umbilical wound should be treated as any other infected wound.

REPORT OF CASE *

History.—A colored girl, aged 7 days, of normal delivery, was seen at the Roper Hospital, Charleston, S. C., in 1927. The onset of the illness occurred at 5 days with stiffness of the limbs and neck. The infant would not nurse and had spasms several times a day.

Examination.—The temperature was 106 F. The eyes were tightly closed and the face was wrinkled (risus sardonicus). There was edema around the lids, trismus and rigidity of the neck. The abdomen was boardlike. The knee reflexes were absent. The umbilical stump was red and swollen, but there was no discharge. The white blood cells numbered 30,520 with polymorphonuclears 70, lymphocytes 26 and monocytes 4. The spinal fluid was cloudy and blood tinged, under slight pressure and contained globulin and 10 cells.

Treatment and Care.—At the time of admission 3 cc. of ampule of 10,000 units of tetanus antitoxin was administered intrathecally, the rest intramuscularly. Calcium bromide 5 grains (0.324 Gm.) and chloral hydrate 2 grains (0.129 Gm.) were administered every four hours for twenty days. Magnesium sulphate (25 per cent), 2 cc., was given intramuscularly once daily for thirteen days.

The infant was tube fed for two days and nursed from the bottle fairly well after that. The temperature went down to normal on the fourth day. Gradual improvement followed until the patient was discharged as cured on the twenty-eighth day.

SUMMARY AND CONCLUSIONS

1. Tetanus neonatorum is not an uncommon disease in the United States.

2. Greater care should be exercised and more stringent laws enforced in regard to the treatment of the umbilical cord after birth.

3. Cerebrospinal meningitis resulting from "sepsis neonatorum" should be differentiated from tetanus neonatorum.

4. The treatment of infants with this disease is mainly symptomatic and is as yet inefficient. Magnesium sulphate seems to give the best results. Tetanus antitoxin has not proved to be of any great value.

5. In those localities in which the disease is common, taking the lives of thousands of infants annually, it would be an interesting and perhaps useful experiment to give a prophylactic dose of tetanus antitoxin to a series of mothers shortly before the birth of the baby and to record the results.

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* The patient in this case was treated by Dr. M. W. Beach, pediatrician to the Roper Hospital, Charleston, S. C., and the case is reported with his permission.

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Case Reports

LIPOID HISTIOCYTOSIS (NIEMANN'S DISEASE) *

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A small group of cases has come to light during the past fifteen years of a condition originally described as Gaucher's disease and more recently established as a distinct clinical and pathologic entity, variously called Niemann's disease, Niemann-Pick's disease, lipoid cell splenohepatomegaly and lipoid histiocytosis. This condition occurs almost entirely in infants of Jewish parentage and affects females more commonly than males, in the ratio of 6:1. It is characterized by slowly progressing emaciation, enlargement of the spleen and liver and death before the age of 2 years from inanition or an intercurrent respiratory infection. Physical and mental retardation are commonly noted, and there are often characters suggesting mongolism or amaurotic family idiocy. Slight enlargement of the lymph nodes and brownish pigmentation of the skin may be present. There is a slight progressive anemia and moderate leukocytosis.

Pathologically, the spleen is firm with rounded borders, and the cut surface is homogeneous with a mottling of yellow or grayish-yellow patches against a dark red background. The liver is distinctly fatty with a bright to dull yellow color, and there is slight generalized enlargement of the lymph nodes, most marked in the abdominal cavity. Microscopically, the outstanding feature is the presence of tremendous numbers of large vacuolated foam cells in the spleen, liver, lymph nodes and bone-marrow and to a less extent in the lungs, suprarenals, thymus, lymphoid structures of the intestines and the central nervous system. These foam cells are large phagocytic cells of reticulo-endothelial tissue origin and are filled with globules of varying size, which give staining reactions consistent with a mixture of true fats and lipoid. The presence of excessive amounts of total lipoids in the spleen and liver has been demonstrated in a few cases by chemical analysis.

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REPORT OF CASE

History.—A Jewish girl, aged 10 months, was taken to the hospital because of vomiting, weakness and failure to gain. The parents were born in Russia. There had been no previous pregnancies, and there were no known familial diseases.

The patient weighed 6 pounds (2.7 Kg.) at birth. She was too weak to nurse, but was given breast milk. For the first four months she seemed fairly well, vomited only occasionally and gained slowly to almost 8 pounds (3.6 Kg.). Throughout the following four months she vomited persistently, and made practically no gain in weight. The vomiting then subsided somewhat, and at 10 months she had gained gradually to 11 pounds (5 Kg.). Her development was thought to be

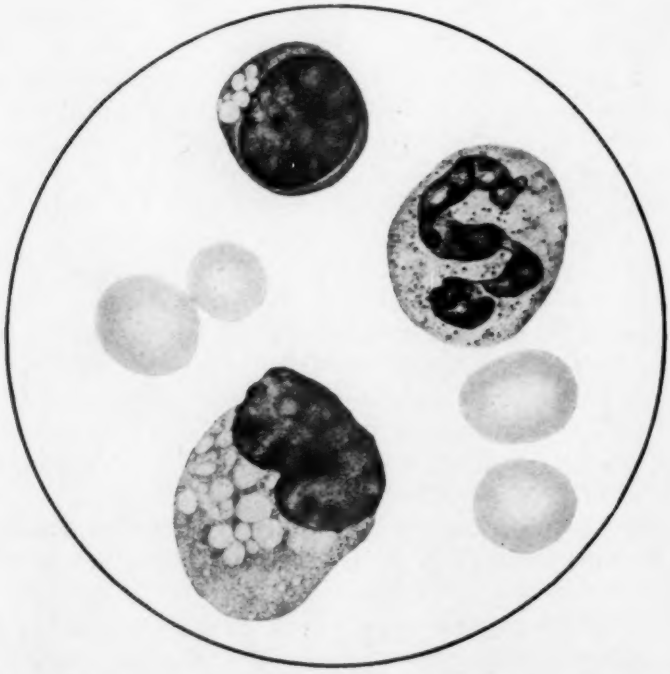

Fig. 1.—Drawing of cells from blood stained by Wright's method, showing a vacuolated lymphocyte and clasmatocyte.

retarded, and she did not sit up. Only three teeth were present, which had appeared when she was 9 months old.

Examination.—On admission to the hospital, physical examination revealed a poorly developed and nourished infant with moderate pallor of the skin and mucous membranes, the former being dry with some desquamation in the axillae. There was slight generalized glandular hypertrophy, and the spleen and liver were moderately enlarged. The musculature was flabby, with apparent atrophy in the gluteal regions. The heart and lungs were essentially normal. The fundi showed no pathologic changes. The patient's stay in the hospital was marked by periods of fever, the temperature at times reaching 104 F. The weight curve showed irregular swings with a constant tendency downward, accompanied by gradual loss of subcutaneous fat, resulting in extreme emaciation. She vomited persistently, and

refeeding by gavage was necessary over long periods. She was given several hypodermoclyses, intravenous infusions of dextrose solution and one transfusion of whole blood, the last being followed by transitory improvement.

A few days after entry, signs of a diffuse pulmonary infection appeared, which was later confirmed by roentgen examination; shortly afterward acute bilateral otitis media developed, requiring incision and drainage. The pulmonary signs persisted to a varying degree throughout the stay in the hospital, as did the aural discharge. She grew progressively worse, and died during the fifteenth week after entry.

The Wassermann reaction of the blood and intradermal tuberculin tests were negative. Repeated blood cultures and agglutination reactions for various organisms to which the elevated temperature might be attributed were negative. The determinations for nonprotein nitrogen, calcium and phosphorus in the blood and the renal function tests were within normal limits. Lumbar puncture yielded normal cerebrospinal fluid. Roentgen examination of the extremities revealed generalized bone atrophy of a mild degree and no localized areas of bone absorption.

There was a moderate secondary anemia and a leukocytosis varying from 12,000 to 35,000. Stained specimens of the peripheral blood were of particular interest, showing a moderate relative and an absolute increase in the lymphocytes and monocytes. The cytoplasm of many of these cells and of a few of the polymorphonuclear neutrophils was vacuolated to a varying degree up to numerous large vacuoles (fig. 1). On one occasion, 27 per cent of the leukocytes contained vacuoles. The abnormal mononuclear cells were fairly large, with somewhat indented, dense nuclei and abundant pale blue cytoplasm without granulations, containing vacuoles of varying size scattered throughout in no definite arrangement. They were negative for oxydase when stained by McJunkin's method, and in supravital preparations with Janus green and neutral red showed the characteristics of clasmatocytes.

Necropsy Observations.—Necropsy was performed seven hours after death. The body measured 66 cm. in length and showed extreme emaciation, with practically no subcutaneous fat. The mesenteric lymph nodes were moderately enlarged, rather soft and grayish. The thymus was pale, not enlarged, and there was no enlargement of the mediastinal lymph glands.

The right pleural cavity was almost completely obliterated by fairly dense, fibrous adhesions. The left pleural cavity contained a few fibrinous and fibrous adhesions posteriorly. There was no free fluid. The right lung weighed 169 Gm. and the left 82 Gm. There was some mucopurulent exudate in the trachea and primary bronchi, and the mucosa was thickened and dull red. There was diffuse consolidation of the entire right lung and nodular consolidation of the posterior portion of the lower lobe of the left lung. The cut surface of the consolidated portions presented a mottled grayish-red appearance. The bronchi were prominent, but there wre no bronchiectatic abscesses and no gross fibrosis or tubercle formation.

The spleen weighed 82 Gm. The external surface was yellowish red and the capsule smooth and glistening. From a distance of a few feet the entire cut surface appeared distinctly yellow. On closer inspection, there was a diffuse mottling of small yellow areas against a dark red back ground. The trabeculae were not prominent, and the corpuscles could not be identified. The surface was greasy to palpation.

The liver was grossly enlarged and weighed 477 Gm. The external and cut surface was light yellow with a diffuse very fine yellowish mottling suggesting fatty infiltration. There were no other changes of note. A thin section was friable and greasy to palpation.

Each kidney weighed 27 Gm. They were pale but otherwise not remarkable.

The suprarenals were pale and appeared to be of normal size. The medulla seemed relatively diminished in amount and was yellowish brown.

The brain weighed 674 Gm. There was some increase in subarachnoid fluid which was slightly cloudy. Direct smear of this fluid showed a few lymphocytes and no organisms. There was no inflammatory reaction or thickening of the meninges. The convolutional markings were normal. There was slight, generalized increase in consistency.

The right middle ear was normal. There was a small amount of thin seropurulent material in the left middle ear, not involving the mastoid spaces.

The vertebral bone-marrow was dark red.

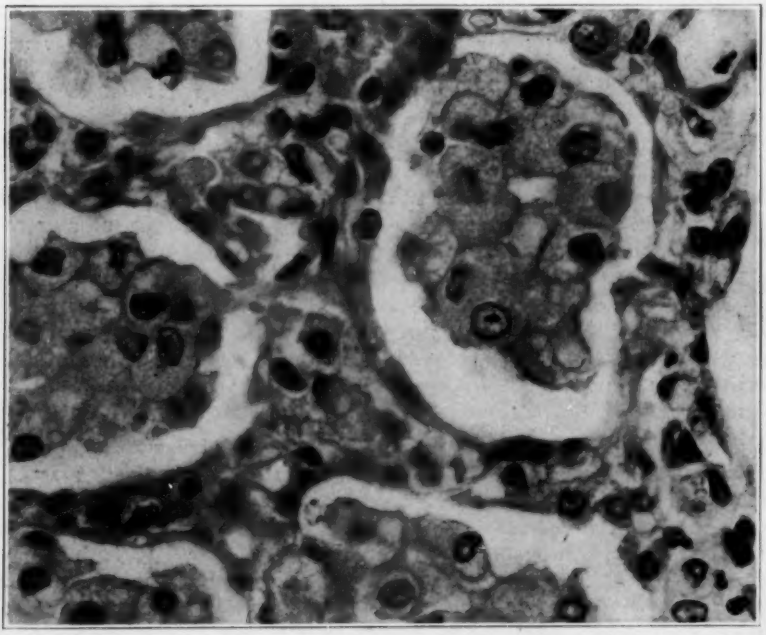

Fig. 2.—Lung. Masses of large foam cells are seen lying free in the alveoli and a few in the alveolar walls. Hematoxylin and eosin; × 700.

Microscopic Examination.—There was fairly extensive, acute and chronic pleuritis and very extensive bronchopneumonia, the bronchial and alveolar exudate consisting chiefly of polymorphonuclear leukocytes. Scattered throughout all sections of the lung, lying free in the alveoli, were tremendous numbers of large round cells, which were uniform in appearance but varied considerably in size, ranging from approximately 20 to 90 microns (fig. 2). They were most numerous in areas in which there was relatively little inflammatory exudate, and completely filled large numbers of the alveoli. There were many round cells in the alveolar walls, apparently free in the connective tissue spaces. The nucleus of these cells tended to be eccentric and was relatively small with from one to three nucleoli and loosely arranged chromatin material. The cytoplasm was pale staining and was filled with many vacuoles of varying size, separated by fine granules and thin strands

of protoplasmic material. Many of the cells were stained pale pink and a few bright orange in scharlach r. In sections stained with hematoxylin and differentiated in a dilute solution of ferric chloride, the cells were clearly defined, staining grayish blue, the vacuoles, however, remaining unstained. Treated with nile blue sulphate, they were stained a delicate lavender. The staining by the Smith-Dietrich method varied from deep blue to black. In sections treated with osmic acid, the foam cells were colored deep black and when mordanted in potassium bichromate before osmication, the staining was much less intense, the cytoplasm presenting a granular appearance.

The structure of the spleen was greatly altered by the invasion of large foam cells similar to those seen in the lungs (fig. 3). These cells were packed together

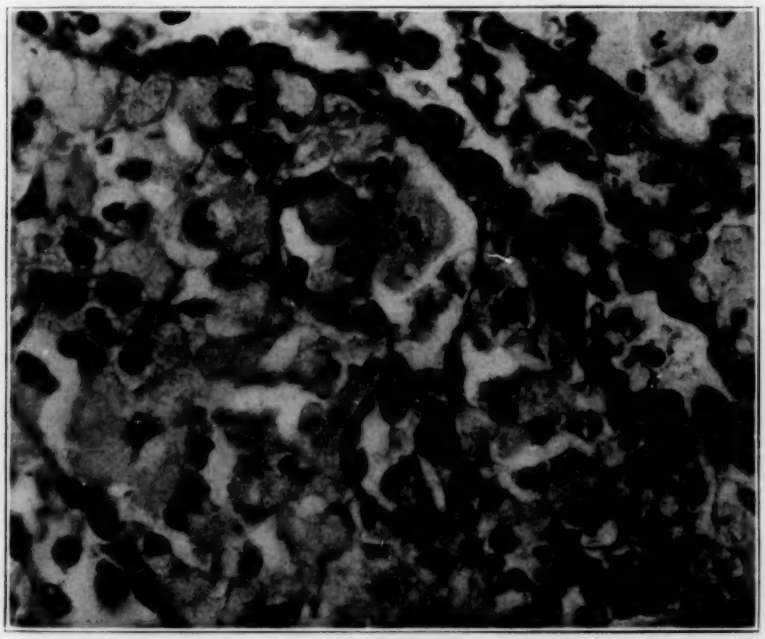

Fig. 3.—Spleen. Large foam cells are seen packed together in the pulp, a few lying free in the sinuses. Hematoxylin and eosin; × 700.

in no definite arrangement throughout the pulp, a few lying free in the sinuses which were prominent as dilated spaces, for the most part empty. The few recognizable germinal centers were composed of an outer zone of small lymphocytes and many centrally placed foam cells mixed with a few small lymphocytes. The nuclei of many of the lymphocytes were pyknotic, and no mitotic figures were present. The trabecular structure appeared normal. The foam cells, examined under polarized light, contained both isotropic and anisotropic substances, the former predominating. In scharlach r the cells stained pale orange, those within the follicles staining somewhat deeper orange. In sections stained with hematoxylin-ferric chloride, the cells were grayish blue, the vacuoles being unstained. Stained with nile blue, they were pale lavender. The most prominent staining of the foam cells was obtained by the Lorrain-Smith-Dietrich method. In these sections they were stained very deep blue, the cytoplasm being filled with minute deep blue

globules, presenting a granular appearance. A deep black stain was produced by osmic acid and after mordanting in bichromate, a much less intense black with a granular distribution.

There was a diffuse vacuolization of the cytoplasm of the alveolar cells of the pancreas, more marked in some areas than in others (fig. 4). These cells did not appear swollen, and the alveolar arrangement was normal. There were no pathologic alterations in the islands of Langerhans. A rare foam cell occurred in the interlobular connective tissue.

There were scattered, small groups of foam cells in the submucosa of the duodenum, chiefly along the muscularis mucosa. No other portions of the intestinal tract were saved for microscopic study.

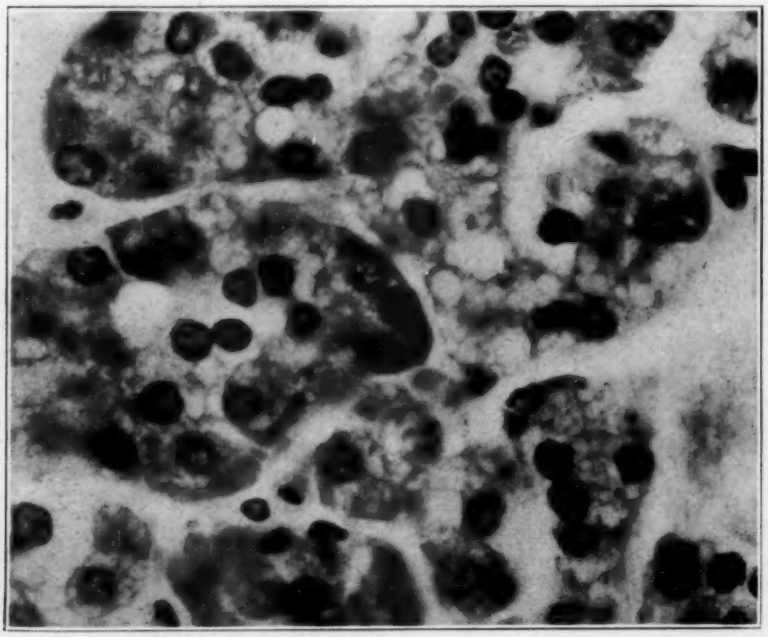

Fig. 4.—Pancreas. Extensive vacuolization of the acinar cells of the gland. There are no foam cells. Hematoxylin and eosin; × 1500.

The sinusoids of the liver were markedly dilated and packed with large foam cells, which in many instances were from two to three times the size of the liver cells (fig. 5). Here the foam cells were polygonal, otherwise being entirely similar to those in the spleen and lungs. A very rare Kupffer cell could be identified, and the sinusoids contained a few erythrocytes. In sections stained with hematoxylin and eosin, the liver cords were narrowed and the cells were pale pink staining in comparison with the grayish foam cells. The cytoplasm was granular and appeared vacuolated. The reaction of the foam cells to fat stains was essentially the same as in the lung and spleen.

A few scattered foam cells were found in the connective tissue at the pelvis and in the glomerular tufts of the kidneys, and there was moderate cloudy swelling of the tubular epithelium.

The medulla of the suprarenal gland was almost entirely replaced by large foam cells, and no normal appearing medullary cells could be identified. The cortical cells were pale staining with granular cytoplasm which in many instances was vacuolated. The foam cells reacted to fat stains similarly to those in the other viscera.

A few foam cells were scattered through the intramuscular connective tissue of the urinary bladder. Three small areas of recent hemorrhage were present in the submucosa.

The architecture of the lymph glands was almost completely masked by the presence of many large vacuolated cells, packed in the marginal and medullary sinuses and scattered through the pulp (fig. 6). The vacuoles tended to be larger

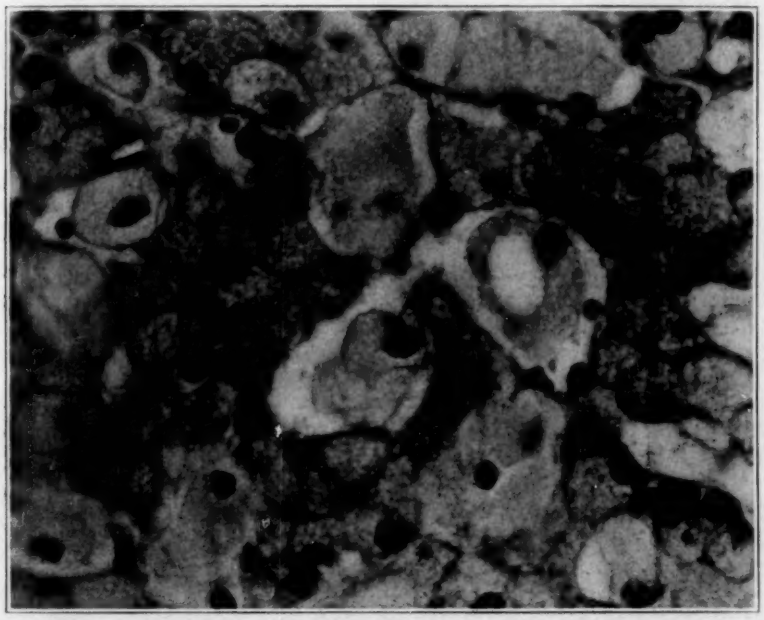

Fig. 5.—Liver. The liver cords are the columns of darker cells filled with small vacuoles giving the cytoplasm a granular appearance. The lighter foam cells are seen packed in the dilated sinusoids. The vacuolization is much less uniform than in the liver cells. Hematoxylin and eosin; × 700.

than in the foam cells of the spleen, and there was giant cell formation in many areas; one tremendously large cell was seen with vacuolated cytoplasm and eighteen nuclei. A few inactive germinal centers could be identified and were composed of numerous large foam cells surrounded by a moderate number of small lymphocytes. There were many neutrophilic leukocytes scattered through the cortical and medullary portions of the glands, and occasional plasma cells and eosinophils were seen. The foam cells of the lymph glands stained pale red in scharlach r, and deep blue in nile blue sulphate. They were stained very deep blue by the Smith-Dietrich method, and when treated with osmic acid stained black, being less intensely stained, with a granular appearance, after mordanting in potassium bichromate.

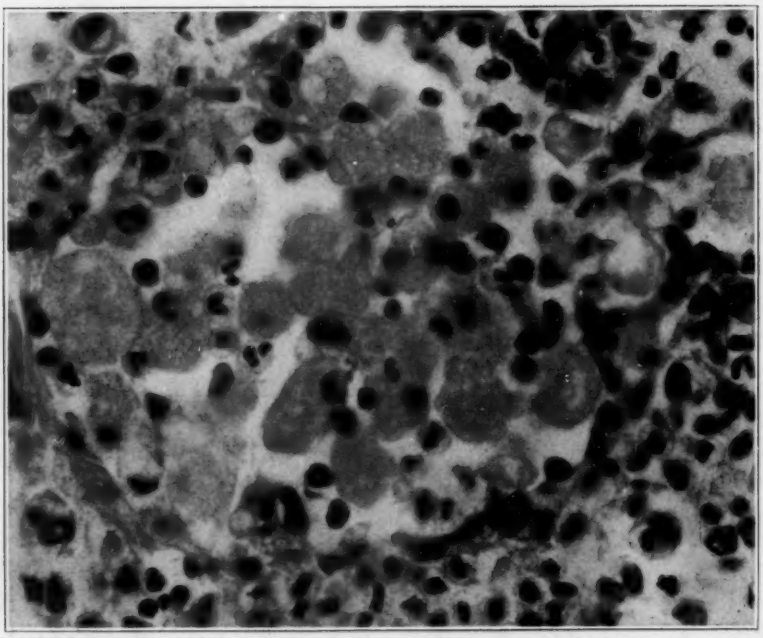

Fig. 6.—Lymph node. Representing a large sinus filled with foam cells. Many polymorphonuclear leukocytes and a relatively few lymphocytes are seen scattered throughout the sinus and reticular tissue. Hematoxylin and eosin; × 700.

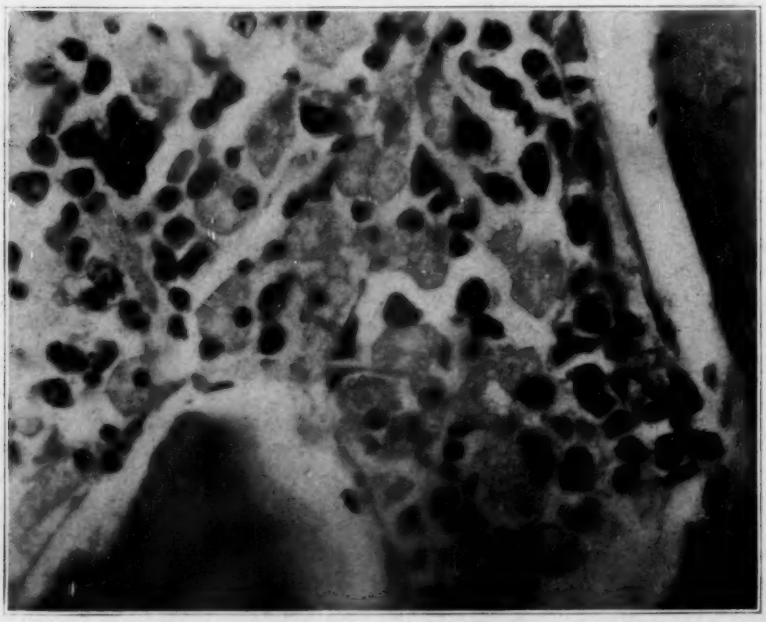

Fig. 7.—Bone-marrow. The marrow cells are almost completely replaced by foam cells which are extravascular. A few scattered small islands of hematopoiesis are seen. Hematoxylin and eosin; × 700.

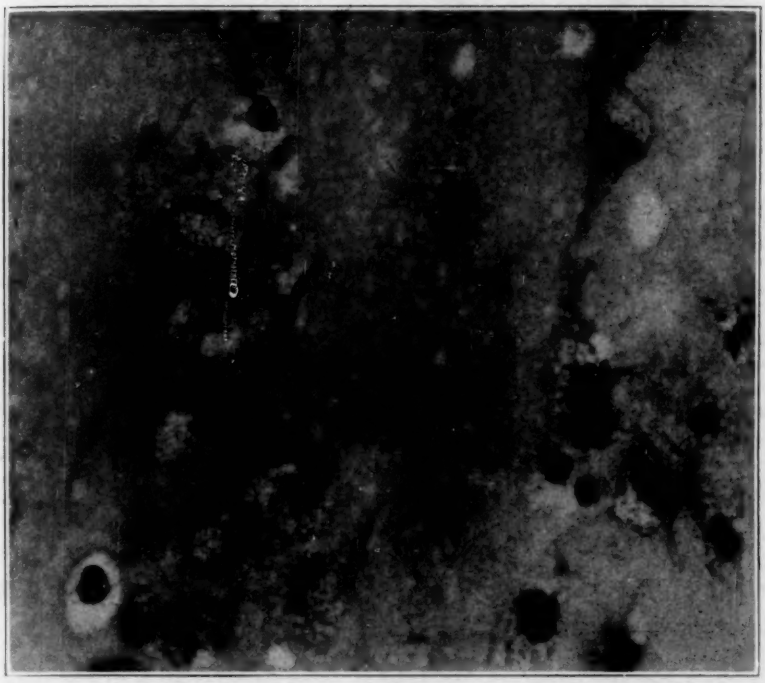

Fig. 8.—Cortex cerebri. The ganglion cells are swollen and vacuolated. Cresylecht violet; × 700.

Fig. 9.—Substantia nigra. Five swollen ganglion cells are shown. Cresylecht violet; × 700.

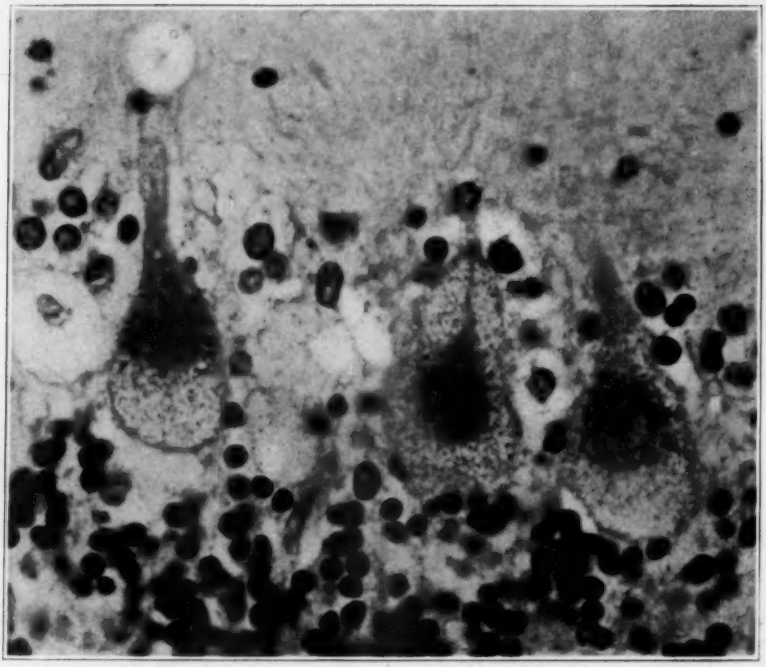

Fig. 10.—Cerebellum. The Purkinje cells are markedly swollen and vacuolated. Cresylecht violet; × 700.

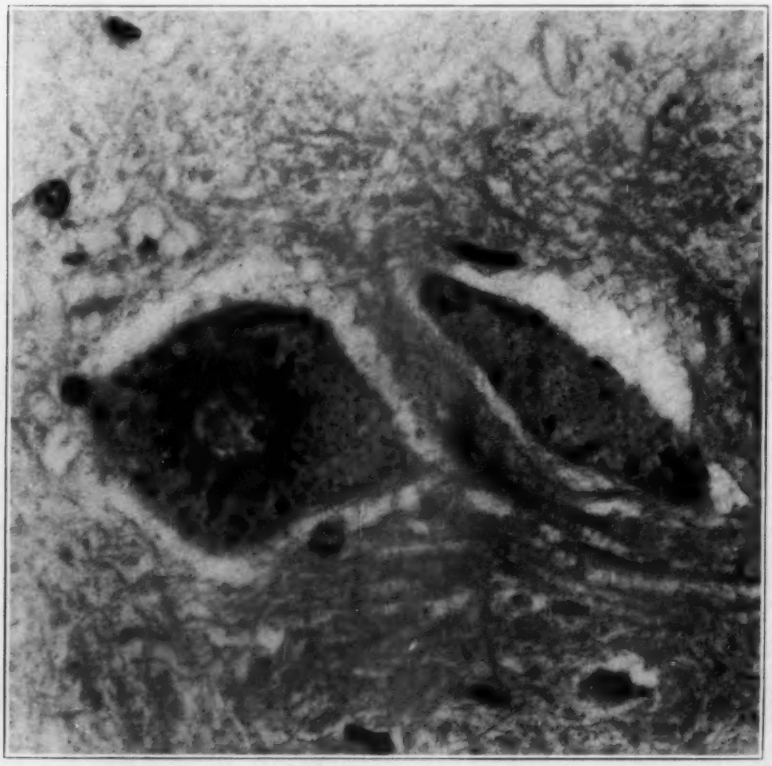

Fig. 11.—Spinal cord. Two anterior horn cells, showing the changes seen in the ganglion cells throughout the central nervous system. Hematoxylin and eosin; × 700.

A tremendous number of large vacuolated cells similar to those in the spleen was present in the bone-marrow, for the most part outside of the capillaries (fig. 7). The marrow was fairly cellular, with scattered islands of hematopoietic activity, the structure being almost completely masked in some areas by the foam cells. Megalokaryocytes were numerous, and the nuclei of many were pyknotic.

Central Nervous System: There was no inflammatory reaction in the meninges, and a few scattered, rather small vacuolated cells were present in the arachnoid and subarachnoid layers (figs. 8 to 11). The ganglion cells throughout the cerebrum, pons and spinal cord and the Purkinje cells of the cerebellum were greatly swollen, some being of tremendous size. Many of the nuclei appeared normal, many were pyknotic and others had disintegrated with loss of the nucleoli. The cytoplasm was filled with minute vacuoles separated by fine filaments of protoplasmic substance, producing a foamy, granular appearance. In a few instances the vacuoles were quite large. The Nissl bodies were fragmented and stained poorly in many of the cells and in others appeared normal. The vacuolization of the ganglion cells was shown most prominently in the Purkinje cells of the cerebellum, which apparently were increased in number. There were a few large vacuolated cells scattered through the layer of cortical cells adjacent to the Purkinje cells, and the former layer appeared thinned out. There was no vacuolization of the small cortical and granule cells. The neuroglia cells showed some involvement.

REVIEW OF THE LITERATURE

In 1914, Niemann [1] reported a case of Gaucher's disease in an infant who died at 18 months. Shortly after this Knox, Wahl and Schmeisser [2] reported two similar cases in infant sisters of Jewish parentage. In one of their patients there were cherry red spots in the macular regions of the retinas, and at necropsy vacuolization of the cortical cells of the brain similar to that seen in amaurotic family idiocy was found. Subsequently, Siegmund [3] reported the fourth case of Gaucher's splenomegaly in infancy. Pick [4] pointed out certain characteristics peculiar to these cases, namely, the age at onset, the racial tendency, the clinical course and the distribution of the large foam cells in the viscera and their reactions to fat stains, and clearly established this group as a clinical and pathologic entity, entirely distinct from Gaucher's disease. He suggested the name, "lipoid cell splenohepatomegaly." Bloom [5] reported two cases of Gaucher's and three of Niemann's disease and stressed the dissimilarities of these two conditions as pointed out by Pick. He proposed the term "lipoid-histiocytosis" to be used to designate this process of unknown etiology which involved the storage of lipoid material in the histiocytes throughout the body. Since these

1. Niemann, A.: Jahrb. f. Kinderh. **79**:1, 1914.
2. Knox, J. H. M.; Wahl, H. R., and Schmeisser, H. C.: Bull. John Hopkins Hosp. **27**:1 (Jan.) 1916.
3. Siegmund, H.: Verhandl. d. deutsch. path. Gesellsch. **18**:58, 1921.
4. Pick, Ludwig: Ergebn. d. inn. Med. u. Kinderh. **29**:519, 1926.
5. Bloom, William: Am. J. Path. **1**:595 (Nov.) 1925.

exhaustive reports, single cases have been published by Henchen,[6] Schiff,[7] Hamburger,[8] Corcan, Oberling and Dienst,[9] Dienst and Hemperl,[10] Kramer and Lederer,[11] Abt and Bloom[12] and Berman.[13] Abrikosoff[14] recently reported "Ein Fall der Skelettform der Niemann-Pickschen Krankheit" in a Jewish girl of 5 years. The age of the patient and the clinical and pathologic observations however, seem more consistent with the syndrome "defects in the membranous bones, diabetes insipidus and exophthalmos," first described in this country by Christian[15] in 1919. Rowland[16] noted the interesting similarities between this condition, Niemann's disease, Gaucher's disease and the large group of xanthomas. He pointed out particularly that high values for blood cholesterol have been obtained in some cases of each of these different groups and that apparently there is an alteration in the lipoid metabolism in each with the deposition of fat substances to a varying degree in the histiocytes of the reticulo-endothelial system and to a less extent in the other cells of the body.

COMMENT

This is the sixteenth case of a rare condition which was first described by Niemann in 1914. Eight of the sixteen have been reported during the past three years. Whether or not this is a new affliction of man, possibly brought about by the change of dietary regimens coincident with the advance of civilization, is an interesting speculation. It seems impossible that had it existed, a condition exhibiting such striking pathologic changes should not have been recognized during the past half century.

The clinical and pathologic observations in this case were practically identical with those in the others reported. Outstanding features were

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6. Henchen, F.: Compt. rend. du XII cong. de méd. des pays du nord, Acta med. Scandinav., suppl. 16, August, 1925, p. 593.

7. Schiff, E.: Jahrb. f. Kinderh. **112**:1 (March) 1926.

8. Hamburger, R.: Jahrb. f. Kinderh. **116**:41 (May) 1927.

9. Corcan, P.; Oberling, C., and Dienst, G.: Rev. franç. de pédiat. **3**:789, 1927.

10. Dienst, G., and Hemperl, H.: Wien. med. Wchnschr. **77**:1597 (Nov. 19) 1927.

11. Kramer, B.: M. Clin. North America **11**:905, 1928. Lederer, M.: Lipoid Cell Splenohepatomegaly (Niemann), Arch. Path. **6**:90 (July) 1928.

12. Abt, A. F., and Bloom, W.: Essential Lipoid Histiocytosis (Type Niemann-Pick), J. A. M. A. **90**:2076 (June 30) 1928.

13. Berman, S. L.: Lipoid Histiocytosis (Niemann-Pick Disease), Am. J. Dis. Child **36**:102 (July) 1928.

14. Abrikosoff, A.: Verhandl. d. deutsch. path. Gesellsch. **23**:101 (April) 1928.

15. Christian, H. A.: Contributions to Medical and Biological Research, New York, Paul B. Hoeber, Inc., 1919, vol. 1, p. 390.

16. Rowland, R. S.: Xanthomatosis and the Reticulo-Endothelial System, Arch. Int. Med. **42**:611 (Nov.) 1928.

the alterations in the circulating leukocytes during life and the changes in the central nervous system at necropsy. The leukocytes showed striking vacuolization, and a large number of clasmatocytes was present in the peripheral blood. In the light of the observations on histologic examination of the tissues, these changes in the circulating leukocytes may be interpreted as a part of the disease process and of diagnostic significance. It is interesting to note in this connection that Abt and Bloom [12] found vacuolization of the leukocytes; I have seen blood smears from two other cases showing similar changes. The ganglion cells throughout the central nervous system were markedly swollen and vacuolated, presenting an appearance similar to that described in amaurotic family idiocy.

The microscopic appearance and the distribution of the foam cells in this case and in those reported by other observers were fairly uniform. There was some variation, however, in the reactions obtained by different staining methods, which may be explained by varying proportions in the substances forming the lipoid content of the cells.

A striking feature of this rare disease of infancy, well illustrated by the present case, is the absence of gross or microscopic evidence of developmental anomalies of any type to explain the symptom-complex. The failure to store fat in the normal depots may be interpreted as an indication of a profound metabolic disturbance. The entire symptomatology, that is, the mental and physical retardation, the failure to gain weight and the anemia, is the secondary effect of such a disturbance, evidenced by the accumulation of lipoid material in the cells of vital organs such as the central nervous system, spleen, liver, lungs and bone-marrow.

DUBOIS' SEQUESTRA OF THE THYMUS GLAND OF NONSYPHILITIC ORIGIN *

E. L. BENJAMIN, M.D.
CHICAGO

Abscesses of the thymus gland were first described by Dubois in 1850 as a product of congenital syphilis. However, twenty-one years earlier, Cruveilhier reported cysts in the thymus gland of infants. Chiari believed that the Dubois abscess was a cyst formed by the thymus tissue invading Hassall's corpuscles, the result of pronounced syphilitic changes. While Schlesinger accepted this view, Tuve held the opinion that the Dubois abscess resulted from necrosis of the medulla of the thymus produced by a syphilitic disturbance in the development of the blood vessels supplying this region. Simmonds and Schridde demonstrated *Spirochaeta pallida* in this lesion. Eberle was not in accord with the opinion of its being a true abscess, but thought that they were dilated epithelial channels, which were remnants of the thymus anlage brought about by a syphilitic vascular disturbance during the development, with subsequent collection of pus in these channels. This explanation was supported by Pappenheimer and Simmonds, Ribbert, and Schmincke. Hammar and Hart called them circumscribed areas of necrosis of the parenchyma of the thymus gland; Hammar spoke of them as sequestrum cysts. If cells are present they are usually lymphocytes and have secondarily migrated into the necrotic areas. The cysts are lined by epithelium which is derived from the ectodermal reticulum. According to Hammar, large sequestrum cysts occur only in congenital syphilis. This is also expressed by Hart, who considers them the result of *Spirochaeta pallida*. Materna described a Dubois abscess in the thymus gland of an African negro, aged 24, suffering from relapsing fever. There were spirochetes (Duttoni) in the wall of the abscess. But this case was questioned by Schmincke.[1] J. Oliver [2] blamed the spirochete of syphilis as being the cause of Dubois' abscesses through the process of degeneration of lymphocytes and Hassall's corpuscles, hypertrophy of the reticulum and dilatation and fusion of the degenerating Hassall's corpuscles to form cysts. In his recent review

* Submitted for publication, Sept. 20, 1929.

* From the Department of Pathology, Cook County Hospital.

1. Schmincke, H., in Lubarsch, O., and Henke, F.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1926, vol. 8, p. 784.

2. Oliver, Jean: Syphilitic Disease of the Thymus in Infants and Mode of Origin in Dubois' Abscesses, Am. J. Dis. Child. **13**:158 (Feb.) 1917.

of the pathologic changes of early congenital syphilis, Schneider [3] considered Dubois' sequestra as specific of syphilis.

It is my purpose in this paper to show that occasionally anatomic lesions indistinguishable from typical Dubois' sequestra may occur in cases in which there is no evidence of their being syphilitic in origin.

REPORT OF CASE

Maternal History.—A white mother, aged 25, in good condition and in the ninth month of her third pregnancy, was admitted to the obstetric ward on Aug. 23, 1928. Her family history was nonessential. Her first child was spontaneously delivered in 1926. Her second infant was a full-term baby delivered by forceps in 1927. Both are living and well. A thyrotoxic crisis had occurred during the second to the seventh month of her third pregnancy which had spontaneously subsided without treatment two months prior to her admission.

On entrance the patient appeared well nourished; the eyes were prominent, and the isthmus of the thyroid gland was moderately enlarged. The Wassermann report of the blood was negative. Vaginal smears were negative. The temperature was 98.6 F.; the pulse rate was 80, and the respiration rate was 20. September 1, the patient normally delivered a full-term male infant weighing 7½ pounds (4 Kg.). The duration of labor was one and one-half hours. The membranes were artificially ruptured, and a brown fluid escaped. The placenta was delivered intact and grossly normal. The blood pressure was 146 systolic and 100 diastolic. The pulse rate was 120 a minute. The basal metabolic rate was plus 33 per cent.

September 2, there were 3,400,000 red blood cells and 10,200 leukocytes, including 76 per cent polymorphonuclear cells, 20 per cent lymphocytes and 4 per cent monocytes. The bleeding time was nine minutes; the coagulation time was two and a half minutes. A constrictor applied around the arm for five minutes, at a pressure of from 90 to 100 mm. of mercury, produced petechial hemorrhages in the skin. The blood pressure was 130 systolic and 84 diastolic. On the eighth day, she was discharged in good condition after an uneventful recovery.

Infant History.—Immediately after the umbilical cord was ligated, a diffuse generalized purple papular cutaneous discoloration was seen in the skin over the entire body of the infant and in the mucous membranes. On closer inspection, these areas measured from 1 to 8 mm. in diameter and looked like blueblack petechial spots. Some of them were slightly elevated and tense, and the epidermis over some had broken, permitting a small amount of bright red blood to ooze from the surface. There was moderate cyanosis of the extremities. The sagittal suture and the posterior fontanel were tightly closed. There was no increase in the thymic dulness. Blood-tinged mucus was present in the mouth. On the second day the petechial spots were more pronounced, and the spleen was distinctly palpable by its firm edge two fingerbreadths below the left costal margin. Large bloody stools were passed. The hemoglobin was 100 per cent, there were 10,200 white and 4,480,000 red cells. There were 10 per cent polymorphonuclears, 82 per cent lymphocytes and 8 per cent monocyte cells. The bleeding time was fifteen minutes; the coagulation time was four and one-half minutes. The temperature was 99 F. The infant died on the third day.

3. Schneider, P.: Die Organveraenderungen bei angeborener Frühsyphilis, Verhandl. d. deutsch. path. Gesellsch. **23**:177, 1928.

Pathologic Report.—Necropsy was performed by Dr. R. H. Jaffe twenty-two hours after death.

The skin, mucous membranes and conjunctivae were diffusely speckled with purple-violet patches, from 1 to 8 mm., with slightly elevated centers, from 1 to 3 mm. in diameter, showing a rough surface containing a soft material which could be easily scraped off. Eighty-five patches were counted over the right arm. The anterior fontanel was 6 by 7 mm.

There were hemorrhages in the leptomeninges, especially about the poles of the temporal lobes. Cortical hemorrhages, 4 by 2 mm. in diameter, were present

Fig. 1.—Dubois' sequestra of thymus gland. Note the central area of necrosis sharply separated from the surrounding thymic tissue. The deeply stained areas in the center are deposits of calcium. Low power magnification. Formaldehyde fixation, paraffin section. Hemalaum-eosin stain.

in the middle and upper parts of the cerebellum. The region of the central ganglions was light yellow. On microscopic examination were seen extensive recent hemorrhages into the cortex of the cerebellum and also the medullary portions, completely destroying the tissue and separated from the surface by a marginal zone.

The thymus weighed 15 Gm., and was deep red and firm. Its transverse diameter was 6 cm.; its longitudinal diameter was 4.5 cm., and the anteroposterior

diameter was 1.5 cm. On cut section numerous soft, pale yellow areas, varying in size from that of a pinpoint to 2 by 12 mm. in diameter, were seen. The material in these areas could be easily removed, leaving irregular cavities with a smooth lining. On microscopic examination, the structure of the thymus was so changed as to obscure completely the normal architecture. The organ was composed of a variety of cells, most of which were myeloid. There were large lymphoid elements with pale-stained nuclei, myelocytes and nucleated red cells. The macroscopically soft yellow areas were foci of necrosis with calcium deposits. They were sharply demarcated and surrounded by proliferating reticulum cells,

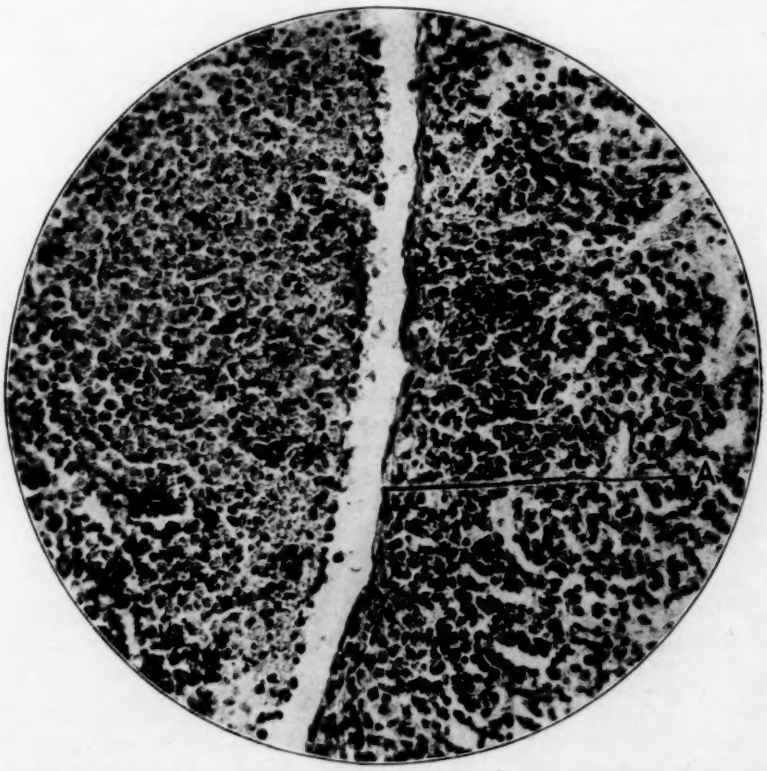

Fig. 2.—Edge of necrotic area showing a thin layer of stratified epithelium (*A*). The necrosis is to the left. High power magnification. Technic same as in figure 1.

which about the larger foci arranged themselves in several layers. The smallest areas had no such lining. There was also much hyperemia and extravasation of the erythrocytes about the necrotic areas.

The spleen weighed 29 Gm. and was covered with a small amount of yellow fibrinous material. Microscopic examination revealed a loosening of the pulp with proliferation and swelling of the reticulum cells and scattered areas of erythropoiesis and granulopoiesis. There were large irregular areas of necrosis surrounded by hemorrhages in the center of which were areas of marked calcification.

Deep red patches were seen in the pyloric region of the stomach and in the urinary bladder. On microscopic examination, the small intestine revealed a

diffuse thickening of the submucosa with marked capillary dilatation and recent hemorrhages. The submucosa consisted of fibrillar connective tissue with numerous swollen fibrocytes and mononuclear elements. In some places the cellular content was very abundant. The large lymph follicles extended close to the muscularis propria, and showed a central proliferation of the reticulum cells with recent hemorrhages. Due to the thickening of the submucosa, the muscular mucosa stood out with marked distinction. The mucosa was greatly affected by postmortem changes. There was a marked hyperemia with an increase of the cellular content.

There was active erythropoiesis in the liver with numerous nests of normoblasts and megaloblasts, and marked hyperemia throughout the tissue. There were cortical degenerative changes in the suprarenal glands, and the formation of small cysts filled with a basophilic substance. The lung revealed extensive hemorrhages into the parenchyma and subpleural space.

In spite of a most careful search, Levaditi preparations made from numerous parts of the thymus, spleen, liver and suprarenal tissues did not reveal any *Spirochaeta pallida*. Various bacteria stains (Gram-Weigert, Unna-Pappenheim) were also negative.

The pathologic anatomic diagnosis was purpura hemorrhagica with recent hemorrhages in the skin and mucous membranes of the mouth, urinary bladder, stomach and intestines; hemorrhagic extravasations into the lungs, liver and kidneys; multiple foci of necrosis (Dubois' sequestra), hemorrhagic extravasations and myeloid metaplasia in the thymus gland; hyperplasia of the mesenteric and peribiliary lymph glands; focal fibrinous perisplenitis; marked hyperemia and tumefaction of the spleen; icteric tint of the visceral organs; hemorrhages in the cerebellum; multiple petechial hemorrhages in the leptomeninges of the basal portion of the brain; degeneration of the cortices of the suprarenal glands; marked anemia of the corporal musculature; cystic dilatation of the lower pole of the right kidney with atrophy of the surrounding medulla and cortex; extramedullary myelopoiesis in the spleen and liver.

COMMENT

Most of the Dubois sequestra previously reported were associated with syphilitic changes in other organs, such as osteochondritis, pneumonia alba or interstitial hepatitis. In this instance there were no such changes. In addition, the history did not show any evidences of a syphilitic infection of the mother. She had two normal children, and her Wassermann reaction was negative. The structure of the thymus gland was masked by hemorrhagic extravasation, myelopoiesis, increase in the reticulum cells and the absence of Hassall's corpuscles. Dubois' sequestra, therefore, cannot always be considered as pathognomonic of congenital syphilis. As to the etiology of the thymic sequestra, in the present case an intra-uterine intoxication, possibly associated in some manner with the thyrotoxicosis of the gravid mother, as evidenced by the purpura hemorrhagica is suggested.

ACUTE MEDIASTINAL ABSCESS *

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Acute abscess of the mediastinum is exceedingly rare in infancy and in childhood. Müller [1] quoted Hare, who reported a series of sixty-six cases gathered from the literature, in which only six patients were in the first decade of life and nine patients in the second decade. Cook [2] reported four cases, in which the patients were 8 months, 8 years, 11 years, and 16 years of age, respectively. Achenbach [3] reported a case in an infant, aged 3 weeks, following sepsis from thrombo-enteritis of the left umbilical artery and grip. Von Dehn [4] reported a case of bilateral empyema with abscess of mediastinum in a child, aged 3 years. I have not found one case of pure mediastinal abscess in the records of the Milwaukee Children's Hospital, although the records of two cases showed acute generalized mediastinitis with death, following tracheotomy and acute retropharyngeal abscess.

The following report may be of interest both from an etiologic and from a therapeutic standpoint.

REPORT OF CASE

H. P., aged 21 months, was in good health except for an occasional cold until Dec. 14, 1928, when she developed a grippal infection of the upper respiratory tract, prevalent at the time. She had a constant temperature of from 100 to 103 F. No Koplik's spots were seen, although the patient was exposed to measles. After twelve days of constant high temperature, she was removed to a hospital. Physical observations of the chest were negative. A roentgenogram of the chest was negative. The leukocytes numbered 21,750, and the polymorphonuclears 83 per cent. A marked distressing cough was present. The next day a typical measles rash appeared. The temperature rose to 105 F., but the leukocyte count remained high (35,150), with 88 per cent polymorphonuclears. The rash gradually faded in four days, but the high temperature and the high leukocyte count persisted. On Jan. 3, 1929, three weeks after the onset of the illness, a roentgenogram revealed a shadow of increased density in the right upper part of the chest, apparently continuous with the mediastinum. On January 5, two days later,

* Submitted for publication, Sept. 26, 1929.

* Read before the Milwaukee Pediatric Society, May 8, 1929.

1. Müller, W.: Mediastinal Abscesse, Zentralbl. f. Chir. **10**:23, 1920.

2. Cook, O. S.: Acute Mediastinal Abscess, Am. J. Roentgenol. **10**:696 (Sept.) 1923.

3. Achenbach, S.: Mediastinal Abscess in 3 Weeks Old Infant, Arch. f. Kinderh. **74**:188 (April) 1924.

4. Von Dehn: Ueber die Mediastinitis Anterior im Roentgenbilde, Berl. klin. Wchnschr. **47**:480 (March) 1910.

bilateral suppurative otitis media developed. Bilateral paracentesis was done. The mediastinal shadow gradually increased in size on repeated roentgen examinations until January 11 (fig. 1). Fluoroscopy and stereoscopic films showed the shadow to be well defined, dense, well inside of the anterior mediastinum and outside the

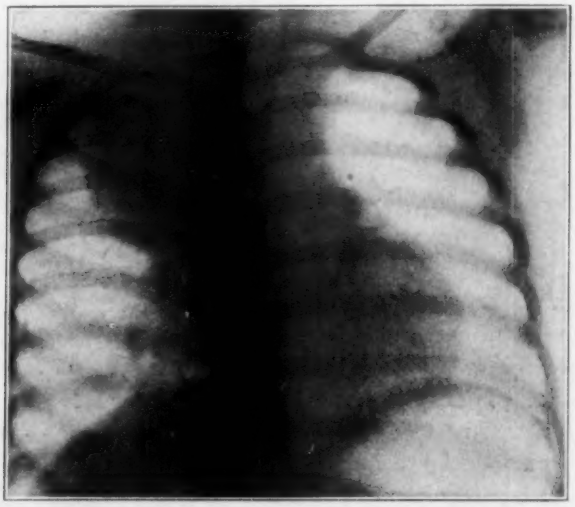

Fig. 1.—A dense stereoscopic shadow is visible well inside of the anterior mediastinum and outside of the lung.

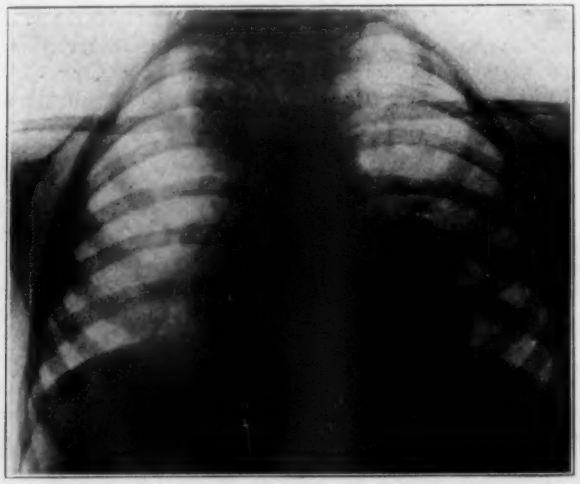

Fig. 2.—Appearance of shadow, after aspirations and ultraviolet ray therapy.

lung. The child was hoarse, had a brassy cough and complained of difficulty in swallowing. The only physical observation in the chest was amphoric breathing over a small area in the second and third intercostal space just to the right of the sternum, about the size of two stethoscope bells. An aspirating needle was inserted in the third right intercostal space, anteriorly, about 2 cm. to the right

of the sternum and directed inward, medianward, and upward for approximately 2¾ inches (7 cm.) before pus was obtained; 45 cc. of thick grayish pus was aspirated, which showed mixed infection of streptococci and pneumococci on culture. A blood culture, the Pirquet test and a urine culture all gave negative results. Hoarseness and difficulty in swallowing were relieved somewhat. Aspirations were repeated every few days. On January 13, 60 cc. of pus was aspirated; on January 15, 45 cc. of pus; on January 17, 30 cc. of pus; on January 20, 10 cc. of pus, and on January 23, no pus. The high temperature, high leukocyte count and dense shadow persisted for a week after the unsuccessful aspiration; then, suddenly the temperature dropped to normal and remained normal. The child was then given general tonic doses of ultraviolet rays every other day. She gained 5 pounds (2.3 Kg.) in weight during the following five weeks. The roentgen shadow gradually became smaller (fig. 2) and finally disappeared (fig. 3). At the present time the child is in excellent condition.

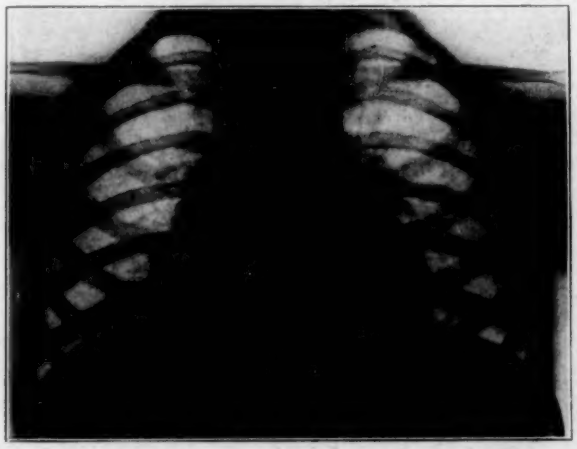

Fig. 3.—Roentgenogram of the patient at the present time, showing normal condition of the chest.

COMMENT

This case of acute mediastinal abscess was probably due to encapsulation of suppurating tracheobronchial lymph glands draining the upper respiratory tract, which was involved in the infection of the upper respiratory tract and in the measles. The mediastinal lymph nodes often become infected in diseases of the respiratory tract, and especially the tracheobronchial groups, which according to Most receive the lymphatics from the lungs, the bronchi, the lower part of the trachea and its bifurcation. An abscess of the tracheobronchial lymph glands may break into a bronchus with recovery, but there are many autopsies reported in the literature in which it was found that abscesses from suppurating lymph nodes had ruptured into one of the large blood vessels, or into the heart and other organs in the mediastinum.

The treatment usually advised in acute abscess of the anterior mediastinum is trephining of the sternum and insertion of a tube or resection of one or more ribs. In this case, however, only repeated aspirations close to the sternum were used and fortunately the case went on to an uneventful recovery.

In addition to the articles referred to in this article I also consulted those included in the bibliography.

425 East Water Street.

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Konjetzny, G. E.: Phlegmonous Mediastinitis and Its Surgical Treatment, Deutsche Ztschr. f. Chir. **197**:108, 1926.

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Ribadeau, L.; Dumas, and Chabrun: Pulmonary Adenitis in Infants, Bull. et mem. Soc. méd. d. hôp. de Paris **51**:402 (March) 1927.

Progress in Pediatrics

SCHILDER'S DISEASE (ENCEPHALITIS PERIAXIALIS DIFFUSA)

A REVIEW OF THE LITERATURE AND REPORT OF A CASE *

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The term diffuse cerebral sclerosis was long applied to a group of diverse diseases characterized by diffuse glial hyperplasia, admittedly the end-result of varied pathologic conditions including inflammatory, degenerative and developmental lesions. In 1912, Schilder [1] isolated from this broad group what he termed a new disease entity, encephalitis periaxialis diffusa, or as it is more commonly termed, Schilder's disease.

His original case was that of a child who presented a confusing clinical picture and died after operation for a presumed cerebral tumor. On the basis of this case and of four other cases that he chose from the literature (those of Ceni,[2] Rossolimo,[3] Beneke,[4] and Haberfield and Spieler [5]), Schilder characterized the new pathologic entity as a sharply delimited but diffuse subcortical symmetrical involvement of the white matter. The myelin sheaths were destroyed with relative preservation of axones, and secondary hyperplasia of the fibrillary glia took place. Profound proliferation of phagocytic glia served to remove the débris and fatty products. Inflammatory signs consisted in large perivascular infiltrations of lymphocytes. In 1913, Schilder [6] published another article on encephalitis periaxialis diffusa in which he described the pathologic anatomy of the case previously described by

* Submitted for publication, Nov. 7, 1929.

* From the Cook County Hospital.

1. Schilder, P.: Zur Kenntnis der sogenannten diffusen Sklerose, Ztschr. f. d. ges. Neurol. u. Psychiat. **10**:1, 1912.

2. Ceni: Ueber einen interessanten Fall gliomatöser Infiltration bei der Grosshirnhemisphären, Arch. f. Psychiat. **21**:809, 1899.

3. Rossolimo: Zur Frage der multiplen Sklerose und Gliose, Deutsche Ztschr. f. Nervenh. **11**:88, 1897.

4. Beneke: Ein Fall hochgradiger und ausgedehnter diffuser Sklerose des Zentralnervensystems, Arch. f. Kinderh. **47**:420, 1908.

5. Haberfield and Spieler: Zur diffusen Sklerose des Hirns und Rückenmarks, Deutsche Ztschr. f. Nervenh. **40**:436, 1910.

6. Schilder: Zur Frage der Encephalitié periaxialis diffusa, Ztschr. f. d. ges. Neurol. u. Psychiat. **15**:359, 1913.

Haberfield and Spieler and added another case from the literature (that of Redlich[7]). In the same year, Krabbe[8] published a case of what he considered an early form of Schilder's disease. In 1914, Marie and Foix,[9] apparently without any knowledge of Schilder's work, reported a similar anatomicopathologic case which they called "Sclérose intracérébrale centro-lobaire et symmétrique." Between the years 1914 and 1924, Jacob,[10] Krabbe,[11] Schröder,[12] Henneberg,[13] Walter,[14] Stauffenberg,[15] Neubürger,[16] Hermel,[17] Braun,[18] Kaltenbach,[19] Klarfield,[20] Siemerling and Creutzfeldt[21] reported similar cases in the German literature, Claude and Lhermitte,[22] and Rochon-Duvignaud and others[23] in the French literature and Gans[24] in the Dutch literature. Nothing

7. Redlich: Demonstration eines Hirntumors mit regressiven Erscheinungen, Wien. klin. Wchnschr. **26**:82, 1913.

8. Krabbe: Beitrage zur Kenntnis der Frühstadien der diffusen Hirnsklerose, Ztschr. f. d. ges. Neurol. u. Psychiat. **20**:108, 1913.

9. Marie and Foix: "Sclérose intracérébrale centro-lobaire et symmétrique," Rev. neurol. **27**:1, 1914.

10. Jacob: Zur Pathologie der diffusen Infiltrationen Encephalomyelitis, Ztschr. f. d. ges. Neurol. u. Psychiat. **27**:290, 1915.

11. Krabbe: A New Infantile Form of Diffuse Brain Sclerosis, Brain **29**:74, 1916.

12. Schröder: Encephalitis und Myelitis, Monatschr. f. Psychiat. u. Neurol. **43**:146, 1918; Neurol. Centralbl. **31**:1048, 1912; **33**:986, 1914.

13. Henneberg: Ueber disseminierte Encephalitis, Neurol. Centralbl. **35**:652 and 984, 1916.

14. Walter: Zur Symptomatologie und Anatomie des diffusen Hirnsklerose, Monatschr. f. Psychiat. u. Neurol. **44**:87, 1918.

15. Stauffenberg: Ein Fall von Encephalitis periaxialis diffusa, Ztschr. f. d. ges. Neurol. u. Psychiat. **39**:556, 1918.

16. Neubürger: Histologisches zur Frage der diffusen Hirnsklerose, Ztschr. f. d. ges. Neurol. u. Psychiat. **73**:336, 1921.

17. Hermel: Ueber einen Fall von Encephalopathica chronica diffusa, Deutsche Ztschr. f. Nervenh. **68-69**:338, 1921.

18. Braun: Ueber einen Fall von diffuser Encephalomyelitis, Ztschr. f. d. ges. Neurol. u. Psychiat., 1922, vol. 80.

19. Kaltenbach: Ueber einen eigenartigen Mackprocess, etc., Ztschr. f. d. ges. Neurol. u. Psychiat. **75**:139, 1922.

20. Klarfield: Zur Frage der subakut verlaufenden diffusen Erkrankungen des Hemisphärenmarks, Allg. Ztschr. f. Psychiat. **79**:294, 1922-1923.

21. Siemerling and Creutzfeldt: Die Formen der Gliablastose und ihre Stellung zur diffusen Hirnsklerose, Ztschr. f. d. ges. Neurol. u. Psychiat. **81**:290, 1923.

22. Claude and Lhermitte: Leuco-encéphalite subaigue à foyers successifs, Encéphale **15**:89, 1920.

23. Rochon-Duvignaud, Jumentié, and Vallière, Vialeix: Cécité à marche rapide avec stase papillaire modérée mort dans le coma avec contractures intenses et généralisées, Rev. neurol. **30**:11, 1923.

24. Gans: Ein Fall von diffuser Sklerose, Nederl. Tijdschr. v. Geneesk. **2**:1043, 1923.

was reported in the English or American medical literature until 1924, when Bouman [25] of Amsterdam and Collier and Greenfield [26] of England reported similar cases. Collier presented his patient publicly as having a case of Schilder's disease and proved it at autopsy. Collier and Greenfield attempted to define the clinical picture of the disease more clearly. They described it as a malady usually occurring in children and young subjects with no tangible causal factors or antecedents:

> The onset is in a few days, the course progressive with some remissions to a fatal issue, the duration from a few months to three years. The chief early sign is cerebral blindness which becomes complete, to which is added mental reduction and increasing spastic paralysis. Unsteadiness from parietal involvement and deafness from temporal involvement may be conspicuous. The amentia increases and passes into coma which terminates the illness. The condition, usually bilateral, may commence on one side or may be confined to one side—the affection commencing bilaterally in the white matter of the occipital lobes spreads forward through the white centers by contiguity.

In his excellent review of the disease, Bouman divided the cases reported in the literature on a pathologic basis into so-called inflammatory and so-called degenerative groups. His criterion for inflammation was the presence of perivascular lymphocytes and plasma cells. Since 1925, additional cases have been reported by the following authors: Urechia, Mihalescu and Elekes,[27] Matzdorff,[28] Schilder,[29] Scholz,[30] Guttman,[31] Flatau,[32] Parodi and Rica,[33] Kraus and Weil,[34] Brock, Carroll and Stevenson,[35] Foix, Bariéty, Baruk and Marie,[36]

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25. Bouman: Encephalitis periaxialis diffusa, Brain **47**:453, 1924.

26. Collier and Greenfield: Brain **47**:489, 1924.

27. Urechia, Mihalescu and Elekes: Encéphalité periaxiale diffuse, Encéphale **19**:617, 1924.

28. Matzdorff: Ztschr. f. d. ges. Neurol. u. Psychiat. **91**:5, 1924; Zentralbl. f. d. ges. Neurol. u. Psychiat. **39**:100, 1924.

29. Schilder: Die Encephalitis periaxialis diffusa, Arch. f. Psychiat. **71**:327, 1924.

30. Scholz: Klinische Untersuchungen bei familiärer diffuser Hirnsklerose in Kindesalter, Ztschr. f. d. ges. Neurol. u. Psychiat. **99**:651, 1925.

31. Guttman: Die diffuse Sklerose, Ztschr. f. d. ges. Neurol. u. Psychiat. **91**:62, 1924.

32. Flatau: Encephaloleucopathica scleroticans progressiva, Encéphale **20**:475, 1925.

33. Parodi and Rica: Contributo alla conoscenza della encephalite periassile diffusa di Schilder, Riv. di patol. nerv. **31**:588, 1926.

34. Kraus and Weil: An Unusual and Protracted Case of Schilder's Disease, J. Nerv. & Ment. Dis. **62**:620, 1925.

35. Brock, Carroll and Stevenson: Encephalitis Periaxialis Diffusa of Schilder, Arch. Neurol. & Psychiat. **15**:297 (March) 1926.

36. Foix, Bariéty, Baruk and Marie: À propos d'un nouveau cas de sclérose intracérébrale, centrolobaire et symmétrique, Rev. neurol. **33**:930, 1926.

Babonneix[37] (no autopsy report), Barré et al.,[38] Stewart et al.,[39] Ferraro,[40] Kogerer,[41] Foix and Marie,[42] Schaltenbrand,[43] d'Antona,[44] Baló,[45] Symonds,[46] Globus and Strauss,[47] Ford and Bumstead,[48] and Shelden, Doyle and Kernohan.[49] These additional reports have somewhat enlarged the conception of the disease. The optic chiasma, the optic nerves and the white matter of the cerebellum or of the spine may also be involved. Scholz, Ferraro and Symonds pointed out the occurrence of the disease in several members of the same family. Although the majority of the reported cases affected infants, children and young adults, no discussion of this disease entity has as yet taken place in the American pediatric literature, and only one article concerning this condition has been published in the *British Journal of Children's Diseases* (Symonds[50]). I shall therefore report what may be considered a typical, rapidly fatal case in its clinical and pathologic details, and give a brief tabulation of all the previously recorded cases, to summarize the known facts concerning the disease.

The pathologic diagnosis of Schilder's disease was made by Roy R. Grinker, whose description of the brain is incorporated.

REPORT OF CASE

History.—A white boy, aged 8, was brought into the Cook County Hospital on June 28, 1926, with the complaints of vomiting, right hemiplegia and aphasia of three months' duration. Prior to the onset, he had been well. Vomiting first

37. Babonneix: Encephalitis periaxialis diffusa, Méd. inf. **32**:326, 1926.

38. Barré, Mourin, Draganesco and Reys: Encéphalité périaxiale diffuse, Rev. neurol. **2**:451, 1926.

39. Stewart, Greenfield and Blandy: Brain **50**:1, 1927.

40. Ferraro, A.: Familiar Form of Encephalitis Periaxialis Diffusa, J. Nerv. & Ment. Dis. **66**:329, 1927.

41. Kogerer: Beitrag zur Kenntnis der Encephalitis periaxialis diffusa, Jahrb. f. Psychiat. u. Neurol. **45**:110, 1927.

42. Foix and Marie: La sclérose cérébrale centro-lobaire, Encéphale **22**:81, 1927.

43. Schaltenbrand, G.: Encephalitis Periaxialis Diffusa, Arch. Neurol. & Psychiat. **18**:944 (Dec.) 1927.

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45. Baló: Encephalitis Periaxialis Concentrica, Arch. Neurol. & Psychiat. **19**: 244 (Feb.) 1928.

46. Symonds, C. P.: A Contribution to the Clinical Study of Schilder's Encephalitis, Brain **51**:24, 1928.

47. Globus and Strauss: Progressive Degenerative Subcortical Encephalopathy, Arch. Neurol. & Psychiat. **20**:1190 (Dec.) 1928.

48. Ford and Bumstead: Encephalitis Periaxialis Diffusa of Schilder, Bull. Johns Hopkins Hosp. **44**:443, 1926.

49. Shelden, Doyle and Kernohan: Encephalitis Periaxialis Diffusa, Arch. Neurol. & Psychiat. **21**:1270 (June) 1929.

50. Symonds, C. P.: Encephalitis Periaxialis Diffusa, Brit. J. Child. Dis. **25**: 839, 1928.

83-95 age-June 1928

occurred from two to four times a day for about a week, followed by a remission of four days. Although associated with a left-sided frontal headache, the vomiting was not projectile. A month later, the speech gradually became indistinct, until articulation was impossible. At about this time, weakness of the right arm was noticed, which gradually increased to complete paralysis, and in about another week the right leg was similarly affected. Although vomiting was infrequent before admission, increasing difficulty in swallowing was observed. The family history was entirely negative; the child was of the eighth pregnancy, and was born and developed normally without previous illness.

Physical Examination.—The physical examination revealed a rather poorly nourished child with well formed head, whose general physical condition afforded no noteworthy objective observation. He lay quietly in bed with extended lower limbs and flexed arms and fingers. His body could not be supported by his legs. There was marked spasticity of the right upper and lower extremities with complete paralysis. The left side was less spastic and was only paretic. Atrophies were not present. The right abdominal reflex was absent, whereas the left was present. All deep reflexes were exaggerated, those of the right upper extremity more so than those of the left. A bilateral ankle clonus was obtained. Sensation seemed unimpaired. The cranial nerves were all normal. A complete motor aphasia was present, but the patient apparently understood what was spoken to him. Death occurred three days after admission, about three months after the onset of the disease.

Laboratory Examination.—Roentgen examination of the skull showed an increase of digitation on the inner table. The spinal fluid pressure was normal. The fluid was clear and showed negative globulin and Wassermann reactions. The cell count was 4 per cubic millimeter. The results of the examinations of the urine and the blood were negative.

Diagnosis.—The clinical diagnosis was a tumor of the brain.

Macroscopic Examination of the Brain.—The meninges of the brain showed injection, and the pial vessels were slightly dilated. The brain was normal in contour, and the sulci and convolutions were of normal configuration. Pressure over the left parietal lobe gave an impression of softening that extended forward to the middle frontal convolutions, where there was a markedly softened area. On the cut surfaces, there was slight dilatation of the third ventricle. The gray matter of both hemispheres was replaced by a soft material which on the left side extended to within 4 cm. of the frontal pole, and the right side of this area ended at the level of the anterior end of the caudate nucleus. The softened area varied in consistency. On the left side, it extended and involved the white matter right to the cortex of the superior portion of the parietal lobe, so that there was only a strip of cortex about 3 mm. in thickness. At this area the consistency of the brain was so soft that the cut surface sank to form a cavity. An area on the left side in the frontal lobe also involved the subcortical tissue and had a honey-comb appearance, with thin, threadlike interwoven strands, the outermost portion of which was less thick than the innermost. The frontal lobe on both sides contained an area which was of fairly normal consistency, but which was dark gray. On the left side, the caudate nucleus was involved in this softened area. The corpus callosum was involved on the left and anterior portion and further back on the right side. The occipital lobes on both sides were not involved in any manner, nor was the white matter discolored. The cerebellum as well as the floor of the fourth ventricle, showed injection.

Microscopic Examination.—The pathologic process exhibited a certain selectivity in that the white matter of the cerebral hemispheres bore the brunt of the

disease. The white substance of the cerebellum and spinal cord was unaffected. That the process also involved the gray matter was evidenced by the involvement of the caudate nucleus seen grossly. However, in the cerebral hemispheres the cortical laminae were sharply demarcated from the underlying severely damaged tissue. The essential type of tissue reaction was present in several variations of severity, ranging from what could be correlated with the gross appearance of simple gray discoloration of the white substance to a softened honey-comb structure.

Fig. 1.—Frontal pole showing the large demyelinized area in the subcortical white matter, sharply delimited from the cortex. Myelin sheath stain; × 2.

Myelin sheaths were profoundly altered. In the most severe stages, they were completely absent, while in earlier lesions they were already altered so far as to give rise to the so-called myelin balls. These were globules of material staining by methods applicable to myelin sheaths, but arranged in irregular formation not at all reminiscent of the original sheathlike structure. At the same stage, the Marchi osmium method revealed many globules staining black. No area affected was early enough to show the early stages of myelin sheath disintegration.

Similarly, the axis cylinders were markedly involved. For the most part, they were completely absent in the tissue affected. In the earlier lesions, remnants of them sometimes were seen in short plump segments or in a coarse argentophilic débris.

The characteristic glia change consisted in even the earliest stage of a profound proliferation of astrocytes. These seemingly multiplied rapidly, giving rise to frequent multinucleated giant cells. Grotesque forms, the so-called monster glia cells, were seen, as well as many normal-appearing protoplasmic astrocytes. In the earliest lesions, this type of glia cell alone was undergoing progressive changes. Strangely enough, at the stage of astrocytic proliferation the myelin sheath and

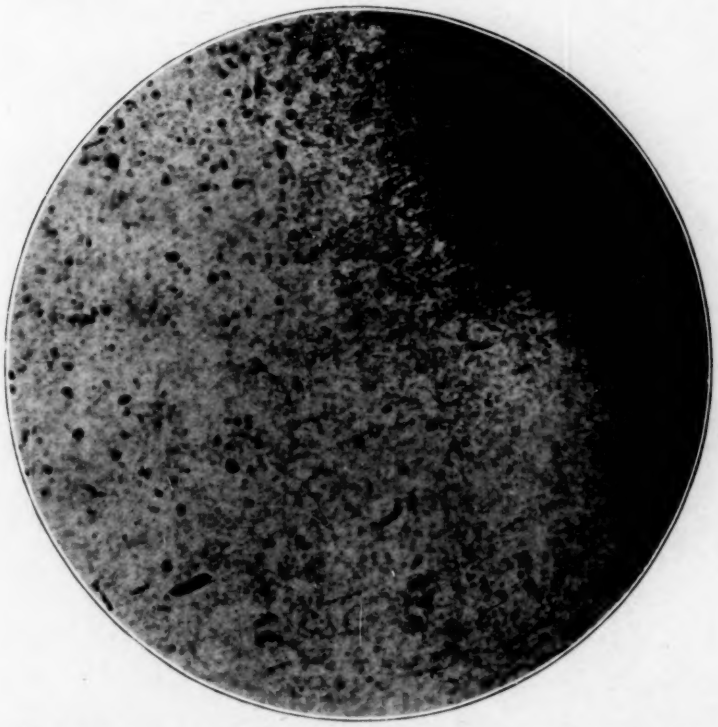

Fig. 2.—Higher magnification of the pathologic area of figure 1, showing the abrupt transition to normal. The involved myelin sheaths are completely destroyed, and only a few balls of myelin substance remain. Myelin stain; × 70.

axis cylinders were already severely degenerated, yet microglia were not in abundance.

In the stage of next severity, the issue had begun to soften and alter its form, in general, to shrink down. At this stage, the microglia underwent rapid proliferation and showed typical formation into gitter cells or phagocytic glia containing fat globules within their cytoplasm. This was accomplished by a rounding up of the nucleus and a shortening and fattening of the processes until the cytoplasm was all present in a large perinuclear structure.

At the same time, the astrocytes were beginning to undergo regressive changes; clasmatodendrosis was plainly visible in that their processes were disintegrated and cut loose from the cell body, forming a granular débris visible in Cajal stain. The cellular cytoplasm rounded out and swelled, the process of which resulted in so-called ameboid cells. The nucleus adopted an eccentric position and shrank and became pyknotic. The cytoplasm showed a homogeneous appearance with all stains, and conformed with what has been called a globoid body or, better, a "gemastete" glia cell.

Still further advances resulted in fine, delicate, central vacuoles appearing in the astrocytic cytoplasm, which stained for fat. Eventually, the entire cell degenerated,

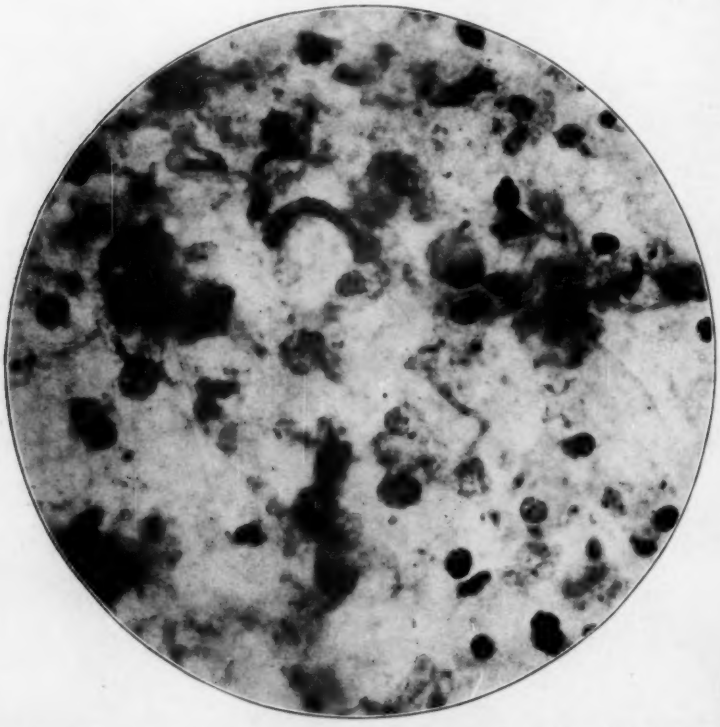

Fig. 3.—The cellular structure of the degenerated areas consists of large fat-filled gitter cells and large proliferated fibrous astrocytes. Toluidine blue; × 550.

leaving in the destroyed area no ectodermal elements. Fat-containing gitter cells were the only cellular content aside from the blood vessels.

During the process of degeneration, the oligodendroglia in the early stages increased in number, but quickly underwent mucinoid degeneration [51] and by their dissolution left free mucin in the tissue.

The gross honey-comb appearance of the white matter in certain areas resulted in an unequal involvement of that tissue. Certain areas still were at the stage

51. Grinker, R. R., and Stevens, E.: Mucoid Degeneration of the Oligodendroglia and the Formation of Free Mucin in the Brain, Arch. Path. **8**:171 (Aug.) 1929.

of astrocytic proliferation with abundant glia fiber network. Between these, other areas had completely softened and had been small enough in size or the process had been slow enough for a complete removal of the débris to have taken place.

The blood vessels were not involved at the onset. Degeneration was not localized to their environment, nor were organic obstructions present. During the course of the softening they were compressed together by the shrinkage of the tissue and were seemingly increased in number. They were surrounded by hordes of fat-containing cells, many of which were incorporated into their adventitial spaces by a proliferation of the adventitial mesh work. Connective tissue pro-

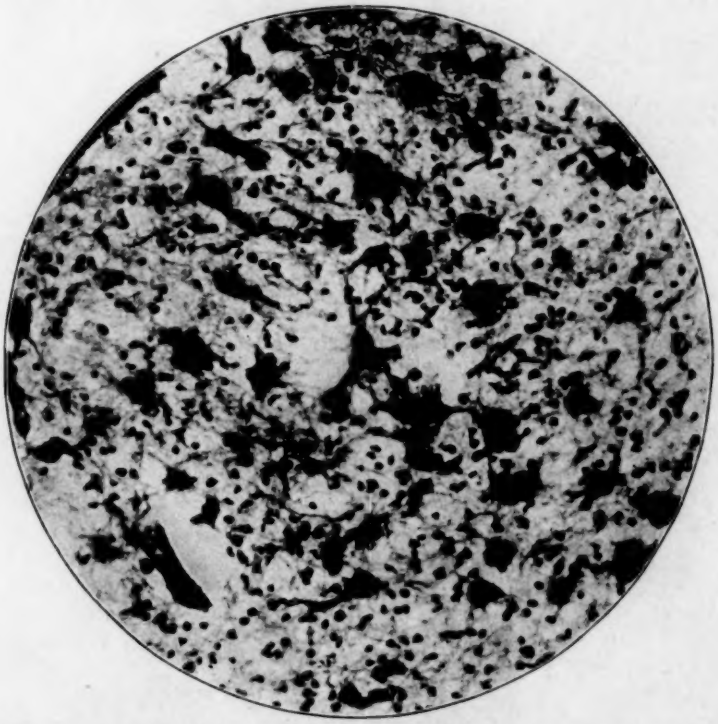

Fig. 4.—An older focus showing the marked proliferation of fibrous astrocytes and the large amount of newly formed glia fibers. Hortegas IV-variant; × 230.

liferation had taken place seemingly from the vessel walls to penetrate the coarse glia network.

Perivascular infiltrations of lymphocytes and plasma cells were frequent and extensive about the vessels in the midst of the softenings. They were, however, not found in normal white substance or cortex and seemed to be greatest where the softening was most profound. No free infiltration of tissue by mesodermal elements was noted.

The leptomeninges were hyperplastic in that the arachnoidal mesh work was increased in thickness and many more histiocytes were found. There was no meningeal infiltrate to be found.

Complete Tabulation of the Cases of Schilder's Disease to the Present Time

No.	Author	Year	Sex and Age	Outstanding Physical and Laboratory Observations	Duration
1	Schilder	1912	Female, 14 years	Gradually developing blindness; vomiting; headache; mental deterioration; right hemiplegia; positive observations on blood and spinal fluid; death after operation for a brain tumor	About 4½ months
2	Schilder	1913	Male, 7 years	Disturbances of vision, walking, speech, leading to blindness; complete spastic diplegia, aphasia and amentia; negative observations on blood and spinal fluid	About 2 years
3	Rossolimo	1897	Male, 16 years	Disturbances of speech, vision and walking; right hemiplegia; death following an operation for a supposed tumor of the brain	About 1 year
4	Ceni	1899	Male, 9 years	Disturbances of vision, speech and gait; finally blindness and complete spastic paraplegia; normal optic disks	About 8 months
5	Beneke	1908	Male, 1¾ years	No clinical history given	
6	Redlich	1913	Female, 41 years	Headaches; disturbances of vision; left-sided paresis; optic neuritis; no observations on spinal fluid given	About 12 months
7	Krabbe	1913	1 year	In a perfectly normal baby acute illness developed, with diarrhea, followed by a rise in temperature, opisthotonos and clonic and tonic spasms; spinal fluid showed traumatic blood; death after 5 days with tuberculous meningitis suspected	
8	Foix and Marie	1914	Female, 18 years	Tetraplegia and loss of speech within 2 weeks, followed later by a recovery; ten years later left spastic hemiplegia and spastic right lower extremity; no observations on spinal fluid given	About 10 years
9	Jacob	1915	Male, 35 years	Disorientation; disturbances of vision and speech; left-sided hemiplegia; finally urinary incontinence and convulsions with death; negative blood and spinal fluid	About 1½ years
10 and 11	Henneberg	1916	Male, 39 years	Forgetfulness, apathy, disturbances of vision, incontinence; bilateral optic neuritis, right-sided anesthesia; no observations on spinal fluid given	9 months
			Male, 43 years	Weakness and paresthesia over the whole left side, leading to a left-sided hemiplegia; two and a half years later diplopia developed; no observations on spinal fluid given	2 years and 8 months
12 to 16	Krabbe	1916	Male, 8 months	Normal delivery; convulsive crying; negative Wassermann reaction; negative spinal fluid; spasticity of extremities; positive Babinski	5 months
			Female, 1 year	Stiffness of the extremities and rigidity of neck noted soon after birth; hyperextension and rigidity of lower extremities; hands and feet in tetanic posture; right disk white and atrophic	About 6 months
			Female, infant	Normal birth; stiffness of the body at age of 6 or 7 months; opisthotonos; vomiting; negative spinal puncture; clonic spasms; negative ophthalmoscopic examination	About 3 months
				Sister with a similar history developed normally during the first months of her life and later showed stiffness of the extremities and tonic spasms and periods of elevated temperature	About 1 year
			Male, infant	Normal delivery; normal development during first 3 to 4 months of life; later rigidity of extremities; negative results in ophthalmoscopic examination	About 6 months
17 and 18	Schröder	1918	Male, 25 years	Epileptic attacks for 3 years; for last 3 months paresis and paresthesia of left lower extremity; spastic paralysis and contractures of lower extremities; negative blood and spinal fluid	3½ years
			Male, 10 years	Enuresis; choreiform movements; apathy; disturbances of vision; spastic paralysis of upper extremities; negative Wassermann reaction	About 1 year
19	Walter	1918	Male, 39 years	Apathy and forgetfulness leading to complete dementia; disturbances of speech and gait; spastic paralysis of lower extremities; negative spinal fluid Wassermann reaction	About 5½ years

Complete Tabulation of the Cases of Schilder's Disease to the Present Time—Continued

No.	Author	Year	Sex and Age	Outstanding Physical and Laboratory Observations	Duration
20	Stauffenberg	1918	Female, 21 years	Disturbances of vision leading to blindness; bilateral hemianopia; psychic disturbances; bilateral spastic paralysis	About 8 months
21	Claude and Lhermitte	1920	Male, 19 years	Psychic disturbances with disturbances of vision leading to blindness; aphasia; agraphia; contractures of legs and later of arms; negative spinal fluid	17 months
22 and 23	Neubürger	1921	Male, 13 years	Psychic disturbances with sudden onset of epileptiform convulsions; acute status epilepticus; negative spinal fluid	Several days
			Female, 4½ years	Loss of vision and disturbances of gait; negative results in ophthalmoscopic examination; negative spinal fluid	18 months
24	Hermel	1921	Female, 3 years	Mental deterioration; disturbances of speech and gait; spastic diplegia; negative spinal fluid	About 1 year
25	Braun	1922	Female, 39 years	Headaches; apathy; disturbances of vision; left hemianopia and hemiparesis; operation performed for tumor of the brain	About 4 months
26	Kaltenbach	1922	Male, 24 years	Psychic disturbances progressing to complete dementia; bilateral spastic paralysis; no spinal fluid observations given	1¼ years
27	Klarfield	1923	Female, 23 years	Headaches, vomiting and mental deterioration; disturbances of vision and gait; left hemianopia; right hemiplegia; aphasia and apraxia; no laboratory data given	1 year
28	Siemerling and Creutzfeldt	1923	Male, 4 years	Bronzing of the skin; urinary incontinence; disturbances of speech and gait; paralysis of all four extremities; epileptiform attacks two days previous to death; no laboratory data given	2 years
29	Cassirer and Lewy	1923	Female, 37 years	Acute onset with convulsions; disturbances of vision progressing to practically complete blindness; negative blood Wassermann reaction; death after operation for a supposed tumor of the brain	9 months
30	Rochon-Duvignaud et al.	1923	Female, 22 years	Bilateral blindness within a few days after onset; headache and slight papilledema; death following an operation	74 days
31	Gans	1923	Female, 25 years	Gradual and progressive disturbance of speech, vision and gait; nystagmus, intention tremor, spasticity of extremities	About 10 years
32 and 33	Bouman	1924	Female, 32 years	Headache, vomiting and disturbance of vision; epileptic attacks; bilateral optic neuritis, hemianopia; operation for a supposed tumor of the brain; negative Wassermann reaction	6 months
			Male, 20 years	Epileptiform attacks; imbecile since childhood; progressive bilateral spastic paralysis	About 5 months
34 and 35	Collier and Greenfield	1924	Male, 7 years	Epileptic attacks; disturbances of speech; blindness; deafness; spastic diplegia; no change in fundi	9 months
			Female, 5 years	Disturbances of vision leading to blindness; progressive ataxia; contractures of all extremities; fundi normal; Wassermann reaction negative	15 months
36	Urechia et al.	1924	Male, 37 years	Headaches; apathy; ataxic gait; paresis of both lower extremities; negative spinal fluid Wassermann reaction	7 months
37	Matzdorff	1924	Male, 64 years	Disturbances of speech and deglutition; spastic paralysis of left side	6 months
38	Guttman	1924	Male, 77 years	Seven years previously three attacks of supposed cerebral hemorrhage; lately psychic disturbances; died of pneumonia; Wassermann reaction negative	7 years
39	Schilder	1924	Female, 37 years	Headache; tremor; disturbances of gait and vision; spastic paralysis of right side; bilateral papilledema; death after operation for supposed tumor	9 months
40 to 44	Scholz	1925	Male, 8½ years	Disturbances of vision, gait and memory; loss of speech; bilateral temporal pallor; spastic contractures; convulsions	3 years
			Male, 8 years	Headache; disturbances of vision and speech; spastic paralysis of right side and paresis of left side; spinal fluid negative	4 years, 10 months
			Male, 7½ years	Loss of vision, hearing and speech; disturbances of gait leading to spastic paralysis	1½ years

Complete Tabulation of the Cases of Schilder's Disease to the Present Time—Continued

No.	Author	Year	Sex and Age	Outstanding Physical and Laboratory Observations	Duration
	Scholz (cont.)		Male, 29 years	Disturbances of speech and gait; no record of examination; death from supposed "urinary poisoning" at age of 36	
			Male, 3 years	Headaches; disturbances of speech and gait; death at age of 60; no autopsy	
45	Flatau	1925	Male, 14 years	Disturbances of hearing and vision leading to deafness and blindness; amentia; paralysis of extremities; optic atrophy; negative Wassermann reaction	About 2 years
46	Kraus and Weil	1925	Male, 47 years	Disturbances of vision; ataxia; bilateral ankle and knee clonus; paresis of seventh cranial nerve; marked Romberg	13 years
47	Parodi and Rica	1926	Male, 48 years	Syphilis at age of 33; diplopia; dysarthria; mental deterioration; headaches; spastic paralysis of right side; atrophy of disks	About 2 months
48	Brock et al.	1926	Male, 9 years	Irritability; intention tremor; disturbances of vision, memory and gait; deafness; right hemianopia; spasticity of all the extremities	15 months
49	Foix, Barièty et al.	1926	Female, 4 years	Diplegia; contractures; atrophy of muscles; exaggerated reflexes; bilateral Babinski; urinary incontinence	About 10 years
50	Babonneix	1926	Male, 8 years	Following scarlet fever, anorexia, headache and apathy; disturbances of speech and gait; dysphagia; spastic quadriplegia; urinary incontinence; negative Wassermann reaction	About 4 months
51	Barré et al.	1926	Female, 19 years	Diplopia; headache; difficulty in walking; right hemiplegia; operation for supposed tumor of the brain; spinal fluid negative	About 3 years
52 to 54	Stewart, Greenfield and Blandy	1927	Male, 8 years	Deafness, mental apathy and later blindness; incontinence; hemiplegia of left side; blood and spinal fluid Wassermann reactions negative	About 1 year
			Female, 3 years	Acute vomiting; later spasticity in the extremities; tremor of hands, arms and jaw; bilateral Babinski; spinal fluid with from 10 to 15 lymphocytes	3½ months
			Female, 43 years	Acute rapidly developing blindness; stupor; optic neuritis; death within 8 days; negative spinal fluid	
55 to 57	Ferraro	1927	Female, 26 years	Mental deterioration; disturbance of gait; scanning speech; intention tremor; bilateral optic atrophy; progressive spastic gait	6 years
			Male, 30 years	Brother; emotional instability; unsteady gait; scanning speech; bitemporal optic pallor	5 years
			Male, 21 years	Brother; depression and at times euphoria; disturbances of vision and gait; scanning speech; pallor of right optic disk; spastic paralysis	10 years
58	Kogerer	1927	Female, 23 years	Psychic disturbances; disturbances of gait and vision leading to blindness; bilateral optic atrophy; paresis of both lower extremities	2 years
59	Foix and Marie	1927	Male, 65 years	Spastic paralysis of the right lower extremity since infancy; positive Babinski	
60	Schaltenbrand	1927	Female, 14 years	Headache; apathy; disturbance of gait and vision; choked disks; right hemiplegia followed by paralysis of left leg; left homonymous hemianopia; motor and sensory aphasia; spinal fluid negative	3 months
61	D'Antona	1927	Female, 34 years	Epileptic attacks; disturbances of vision; psychic disturbances; hemiplegia of the left side	
62	Baló	1928	Male, 23 years	Aphasia; agraphia; hemiplegia of right side, and paresis of the inferior branch of the facial nerve; urinary and fecal incontinence; death soon after an operation for supposed tumor of the brain	About 4 months
63	Symonds	1928	Male, 6 years	Difficulty in walking; urinary incontinence; double spastic hemiplegia; negative blood and spinal fluid	About 5 months
64	Globus and Strauss	1922	Male, 3½ years	Gradually developing difficulty in walking; spasticity of the arms, loss of speech and convulsive twitchings four days before admission to the hospital	

Complete Tabulation of the Cases of Schilder's Disease to the Present Time—Continued

No.	Author	Year	Sex and Age	Outstanding Physical and Laboratory Observations	Duration
65 to 67	Globus and Strauss	1928	Male, 1 year	Otitis media and convulsions; rigid extremities; blindness; bilateral optic atrophy; negative spinal fluid	8 months
			Female, 9 months	Spasticity of extremities; right otitis media; rigidity of neck; convulsive seizures; spinal fluid negative	16 days
			Female, 6½ months	Acute vomiting; generalized rigidity; negative cerebrospinal fluid	14 days
68 and 69	Ford and Bumstead	1929	14 years	Headache; internal squint; weakness of both legs and of left arm; bulbar palsy; bilateral Babinski; papilledema; spinal fluid Wassermann reaction negative	About 6 weeks
			Male, 2 years	At 3 years of age, paralysis of both legs, slight weakness of the arms, speech defect, left sixth nerve palsy, bilateral Babinski and stupor; operation for exploration of the posterior fossa; negative spinal fluid	About 1 year
70 and 71	Shelden, Doyle and Kernohan	....	Male, 7 years	Deafness; apathy; bilateral paralysis; blindness	About 8 months
			Female, 27 years	Blindness; negative laboratory data; hemiplegia; death following operation for abscess of the brain	About 1½ months

COMMENT AND CONCLUSIONS

Dr. Grinker's description of the pathologic changes made for the anatomic diagnosis of Schilder's disease. The interpretation of the pathologic observations in relation to the pathogenesis is difficult. Although seventy-one cases are reported and designated as Schilder's disease, both clinically and anatomically they present great variations. This was just as true in Schilder's publications.

A sufficient number of cases is known, however, which present the typical pathologic picture, of which the case reported is a good example. These are characterized by bilateral symmetrical softenings limited to the white substance in which myelin sheaths and axis cylinders are alike affected and with a characteristic proliferation and later degeneration of the astrocytes. The case reported is atypical in that the brunt of the disease was borne by the parietal lobes and the occipital lobes were least affected.

In classifying the disease, the greatest difficulty has been met in determining whether it is strictly a degenerative disease or an inflammatory disease, such as may be due to a virus. The point of departure of these two views as exemplified, on the one hand, in the study by Globus and Strauss [47] and on the other in that by Schaltenbrand [43] is the interpretation of the perivascular infiltration. Is this a sign of inflammation in the narrow sense of the word (infection) or is it a secondary reaction to the destruction of tissue? This is as difficult of answer as in multiple sclerosis.

The perivascular infiltration is found greatest where the softenings are farthest advanced and are absent entirely in the early lesions. This, when compared with the tissue reactions in the softenings following vascular occlusions, is evidence enough that such infiltrations are in

response to the damage of tissue and not part of an inflammatory (defense) reaction to a virus.

I am in sympathy with the term coined by Globus and Strauss of progressive degenerative subcortical encephalopathy if it is an attempt at being agnostic as to the fundamental etiology of the disease. However, I feel that the term Schilder's disease is superior in that it has already been embedded firmly in the literature and in that it avoids the unwarranted dogma of the authors just cited that the disease is purely degenerative.

My own impressions from this study have been of the striking similarity in the finer pathologic details of certain vascular disturbances. The initial proliferation of astrocytes and later their regressive changes, with the absence of proliferation of microglia, are similar to those cortical changes described by Hiller and Grinker.[52] Furthermore, just as in those cases a sharp demarcation existed between pathologic cortex and normal cortex and normal white matter, so here a sharp line existed between pathologic white matter and normal white matter and normal cortex.

It is thus natural that one considers the possibility of a relation of the vascular supply to the softenings. In multiple sclerosis, such a relationship is more obvious because of the small size of the lesions and frequent slow tempo of the process. In Schilder's group, in which the lesions are widespread and the progression rapid to a fatal termination, such relationship is less obvious and has not been conclusively proved. Yet the white substance has a blood supply basically different from that of the cortex. Its main vascular supply arises from the basilar vessels, and its capillary network is far from rich. It seems worthy of suggestion that the disease is a degenerative condition, not as a result of circulating toxins, as Krabbe postulated, nor of a heredodegenerative nature, as is Friedreich's disease, but as a result of vascular disturbances of the white substance.

Because of the massive and variable involvement of the white substance of the brain, a protean symptomatology is to be expected, one difficult of analysis and classification into a syndrome. From the published reports, a general statement may be made as to the general disease picture.

The condition affects males more than females in about the ratio of two to one. Over half the cases occurred before the age of 14 and most before the age of 21. A few cases in adults, even middle aged adults, have been recorded.

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52. Hiller, F., and Grinker, R. R.: Comparison of the Brain Changes Following Organic and Functional Vascular Lesions, to be published.

The onset is variable, being acute or gradual. The majority of cases show no direct relationship to any form of injury, trauma, congenital abnormality, other systemic disease, infection or epidemic. The course is usually steadily and continuously toward a fatal termination usually in a short time, although cases are reported as having a duration of from a few days to thirteen years.

Changes in the mental and psychic status are present almost invariably. When the lesion takes its origin in the more posterior regions of the brain, the mental changes appear in the later stages of the disease. Apathy is a frequent symptom. Hallucinations, loss of memory, disorientation and finally complete dementia have been frequently observed.

Because of the mental changes, accurate sensory examinations are infrequent. However, all variations of sensory losses have been observed. Disturbances of vision form one of the most prominent and frequent symptoms. Complete blindness or partial field defects occur almost invariably. This is associated with normal pupillary reaction and normal conditions of the disks, thus making a diagnosis of central blindness. Since the most frequent origin of the lesion is in the occipital lobes, this bilateral central blindness is a valuable diagnostic sign. Central deafness, although less frequent, is equally suggestive.

Almost invariably signs of involvement of the subcortical efferent fibers are found and vary, depending on the lesion. Monoplegia, hemiplegia and quadriplegia of the spastic type are present. The latter is frequent, since the process is usually diffusedly bilateral. Increased deep reflexes, extensive plantar response, absent abdominal reflexes and incontinence accompany this involvement.

Headache and vomiting frequently occur and are a source of great diagnostic difficulty. This is especially true in view of the occasional papilledema which is present to as high a degree as 3 diopters. Spinal fluid pressure is increased frequently, and the fluid often reveals an increased globulin and cell count.

The diagnostic difficulties are, quite apparently, extremely difficult in the early stages of the disease. Later, when evidence of bilateral diffuse subcortical involvement is manifested which has steadily and rapidly progressed after an acute onset, Schilder's disease must be considered. Spastic quadriplegia, central blindness or deafness, mental apathy and generalized convulsions are the most frequent observations.

Pediatric Biographies

NILS ROSÉN VON ROSENSTEIN

1706-1773

JOHN RUHRÄH, M.D.
BALTIMORE

Nils Rosén von Rosenstein was born near Gothenburg on Feb. 1, 1706 (old style). His father was Erich Rosenius, at the time an army chaplain, and his mother Anna Wekander, who came out of an exemplary family of clergymen. One of his brothers, Eberhard, became professor of medicine at Lund and was subsequently ennobled and took the name Rosenblad.

An anecdote on von Rosenstein's childhood, with which he used to entertain his friends, was that at the age of 4 he was stricken with plague and that he lay over twenty-four hours as dead. His mother, arranging his burial clothes, noticed signs of life and fainted.

In 1718, he attended the Gymnasium in Gothenburg, and two years later the Academy in Lund. His father intended him to enter the ministry, but from his early years he was inclined to the study of medicine. One of his early teachers in medicine was Kilian Stobåus.

His father was not able to allow him much money, so that when he went to Stockholm in 1724 he had to make his way by tutoring, translating and writing for booksellers. In 1728, an adjunct in medicine became vacant and he was regarded as the most suitable applicant; he obtained the position after defending in a contest the theme "de usu methodi mechanicae in medicina." In the following year he and a companion started on two years' travel. His journeying led him through Greifswald, Stettin, Berlin, Wittenberg and Leipzig. Then he spent nearly a year in Halle studying medicine with Friedrich Hoffman, anatomy with Bass and Becker and chemistry with Stabel. He then returned to Leipzig to hear the lectures of Platner; from there he went to Dresden, Cassel, Marburg, Giessen, Frankfort on the Main and Strassburg. He traveled as a scholar and was received everywhere with respect. His travels continued to Besançon and Geneva, Turin, Lyon, Montpellier and finally Paris. After staying in Paris awhile, he pushed on to Brussels and Utrecht where he became friendly with Muschenbrack and von der Schacht. He then visited Amsterdam, Haarlem, Leyden and The Hague in turn, but he returned to Leyden on account of Boerhaave and met Albinus and the naturalist S'Gravesand. In Amsterdam he came in contact with the well read

Le Clerc and Tronchin, and he visited Hardewych to meet de Gorter, at whose hands he received his doctorat, after defending the theme "de historüs morborum conscribendis." On his way back to Sweden, he went through Westphalia, Bremen, Hamburg, Wiemar, Rostock, Stralsund, Ystad and Lund.

In the spring of 1731, he took up his position as adjunct, and now his duties were increased by giving the lectures of the Archiater Rudbeck, who was otherwise occupied in writing a book. From 1731 to 1740, he exercised these offices and was regarded as the foremost teacher of medicine in Upsala. He was about this time made a member of the learned society of the place, the Societas Litteraria. Largely through his teaching Sweden began to be filled with native physicians, and but few foreigners found it advantageous to practice medicine in Sweden.

In 1734, King Frederick appointed von Rosenstein Assesor of the College of Physicians and conferred on him the title of Leibarzt. In 1740, von Rosenstein declined the honorarium offered him as personal physician to the king, as he preferred an academic life to one at court. Another honor was his election as one of the first members of the Royal Academy of Sciences of Stockholm, which was founded in 1739.

The influence of Linnaeus was great in those days, and many physicians were learned not only in medicine but in botany; to this goodly company belonged von Rosenstein. His popularity lay chiefly in the fact that he combined in a remarkably successful way the gifts of academic teaching with the practice of medicine as an art. As a teacher he was eloquent in the lecture hall and he led his pupils from the class room to the wards where he gave bedside instruction. His pupils were always in his thoughts. He entertained them in his house not only talking over medical and scientific subjects but discussing the needs and ambitions of the students themselves. When they were absent he kept in touch with them through correspondence. He was responsible for founding the hospital in connection with the medical teaching, and he contributed much to the development of the apothecaries' art.

In 1733, he treated King Frederick the first for stone, with good results. He watched over the health of Gustav the third, as the biographer naively puts it "before His Highness saw the light," and for this he was made archiater and given a pension from the crown and another from the kingdom. In 1748, King Frederick offered to make him a nobleman, in company with a number of others, and to confer on him the title of Court Intendant, but he refused both. It is also noted that in 1769, with others, he attended the young king, who had smallpox, for which service he was given 10,000 riksdaler. In 1757, he had been given the Royal Order of the North Star. In 1762, the widow queen ennobled him, and Rosén became von Rosenstein with

the proper armorial. His portrait by the artist L'Archevegere was cast in a medallion with those of Linnaeus, Swab, de Geer, and Wallerius.

He was married in 1734 and had three children, only one of whom survived him, Nils von Rosenstein. He died on July 16, 1773, at the

Des Herrn
Nils Roſen von Roſenſtein
Königl. Schwediſchen Archiaters und Ritters
vom Nordſternorden

Anweiſung
zur Kenntniß und Cur
der
Kinderkrankheiten

aus
dem Schwediſchen überſetzt
und mit Anmerkungen erläutert
von
Johann Andreas Murray D.
Profeſſorn der Medicin auf der Akademie
zu Göttingen.

Gotha und Göttingen
bey Johann Chriſtian Dieterich
1766.

Title page of von Rosenstein's work (German edition).

age of 67, and was buried in the Cathedral at Upsala where tablets mark his resting place and that of his son Nils.

Von Rosenstein was not as prolific a writer as many of his contemporaries, as his time was evidently overfilled with his court and academic duties as well as his practice. His contributions to the

academy include forty-six dissertations. His longer contributions include a work on anatomy "Compendium, anatomicum, eller beskrifning om delarne af hela menniskans Kropp," published in Stockholm in 1738.

A popular work written for the king entitled, "Hus och Rese Apoteque på Hennes Kungliga Majestäts nådigaste befallning upsatt," was published in Stockholm in 1765.

And most important of all his work on diseases of children is a book entitled, "Underrätelse om Barns Sjukdomar och deras Botemedel." The first edition appeared from time to time in the Swedish Calendar from 1753 on. The book had an unprecedented success and was published in numerous editions and translations. The list is impressive, and it is doubtful if any other book on diseases of children ever attained such widespread distribution and popularity.

1753	first Swedish
1759	Danish
1764	Swedish
1766	German
1768	German
1768	Dutch
1771	Swedish
1774	German
1776	English
1778	French
1781	German
1785	German
1785	Italian
1793	German
1794	Hungarian
1828	Swedish
1851	Swedish

The German edition of 1785 contains a short account of his life.

This book on diseases of children is the best of its kind previous to 1800. It is full of sound observation and common sense and contains much that is commendable. One of the best chapters is on smallpox, and it will be a revelation to the present day physician unfamiliar with this disease. His observations on prognosis must suffice as an illustration:

> Young people go through this disease with more facility than old persons, and the younger they are, the more successful generally is the cure. Nevertheless we have instances of children, who have got a malignant sort of small-pox, and died, tho' they still were not weakened; but the fault may then lay in the nurse, or nursekeeper; for instance, how should the child be preserved, if the nurse at that time eats much meat, is of a bad temper, or is in love; or if she has her menses, sits in a place to swaddle the child exposed to the draught of air, or swaddle it seldom, and that in linen not warmed, tho' it should have wet itself; or if she lies down on the floor, and takes the child by her, &c. If this besides happens at the

time of teething, the child can hardly by any means be recovered; if the pocks settle in its mouth and throat, or on the lips, it is thereby prevented from sucking. The most favourable age for a patient in the small-pox, is from the fourth year to the fourteenth, and the next favourable one from the 16th to the 25th.

I have myself observed fat children to be as often favoured with a mild kind as lean ones.

If the pustules being licked, have a salt taste, the child that has them, is commonly expected to die, but not else. It is likewise said, that the disease will be severe, if the hands and feet shiver in the first *stadium*, or period, on their being touched: if those who have fed well, lose much blood just before their falling in, either by wounds or otherwise, they will commonly have a favourable small-pox.

It is no good sign if a looseness comes on, just at the time of eruption, and continues still some days during the breaking out of the pustules. If the pocks itch immediately after their coming out, they will not be mild. When the pain in the loins, and the vomiting is gentle, no very offensive smell comes from the mouth, the nose not obstructed, and the throat clean, the small-pox will then be benign, *et e contra.*

Haemorrhages of the lungs, and of the anus, are threatening signs; but the blood being voided along with the urine, not one patient among a thousand will recover. In the small-pox, attended with petechial spots, three sick are sometimes carried off out of four. A confluent small-pox kills sometimes every fourth or fifth of those thus affected.

We fear a bad event if the pustules in the face are flat, and have a depression in the middle, together with a black spot, and if their basis either be dark red or pale, and indolent in the third period; not round and hard to the touch, but soft, as also to the appearance, as if they were wrinkled or empty. Neither can we hope for any good success, if the patient frequently makes water, and but very little at a time; if the urine then looks pale, *delirium* and convulsions are imminent, unless the patient has lately been blistered with a plaister of cantharides.

A diarrhoea in the three first periods does no good, but is often of service in the fourth period; but if that which is carried off looks purulent, or is mixed with blood, or is black, the belly being distended and swelled with some pain, then a gangrene has already taken place in the bowels: it is bad if the suppurative fever does not come on by degrees, but all at once, and with a hard pulse, pain in the head and eyes, which are red for want of sleep (agrypnia), and much uneasiness: if we then observe a hard pulsation in the arteries on the neck, a *delirium* will follow; but death itself is generally the consequence, when the pulse at the wrist of the hand is low at the time the above-mentioned blood vessels are beating hard.

If not only the whole face, but the eye-brows and the lips swell, it is a bad sign; but the patient will very soon die, if the tumour or swelling of the face withdraws hastily, and does not immediately go to the hands; if the spitting ceases, the skin which is between the pustules and their bases turns pale, he likewise being short of breath, his voice altered, with a peculiar hoarseness, and if he is also observed to be forgetful.

When he has many pustules in his throat, what he drinks returns through the nose. This is the cause of children being so much against drinking during the small-pox, and is in that respect chiefly dangerous, as they cannot take the medicines, though in this disease, unless we drink plentifully, death ensues.

A severe cold coming on while the disease is still in its third period, will easily suppress the spitting in a severe small-pox; many are saved by getting large boils, provided they are observed and opened in time.

News and Comment

SOCIETY NEWS

Second International Pediatric Congress, Stockholm, August, 1930 (Second Announcement).—Their Royal Highnesses, the Crown Prince and the Crown Princess of Sweden have graciously promised the convention their patronage.

On special request from several quarters, the date of the convention has been put forward one day, and the new dates are thus Aug. 18 to 21, 1930.

Acting on the suggestions received from the national committees of the different countries, the Swedish organization committee has chosen the following subjects for discussion: (*a*) the biologic effect of direct and indirect ultraviolet irradiation; (*b*) the physiologic and pathologic significance of the thymolymphatic system; (*c*) the psychology and pathopsychology of childhood; their significance as a branch of pediatric research and teaching, and their application in medicosocial work.

The names of the speakers on these subjects will be announced in the near future, as well as the names of those announced in advance by their respective national committees as intending to take part in the discussion. (Free discussion will follow the lectures and discussions by the announced speakers.)

Notification of free lectures should be in the hands of the Swedish organization committee on April 1, 1930, at the latest.

The following time limits for each speaker (subject to change) have been decided on: reports, forty; discussion by announced speakers of the subjects reported, ten; free discussion of the subject reported, five; free lectures, from fifteen to twenty, and discussion of the free lectures, five minutes.

Free lectures should be on investigations not published before.

The fee of admission is twenty Swedish crowns for regular members, and ten crowns for members of their families.

Following the convention, three pleasure trips are being planned for those visiting the convention: (*a*) Stockholm—Dalecarlia (Falun, Lake Siljan)—Gothenburg or Stockholm; duration of trip about two days; price one hundred and twenty crowns, covering second class railway accommodations, board and lodging, guides and tips; (*b*) Stockholm—Jämtland—Trondhjem—Stockholm; about three and one-half days; price two hundred and twenty-five crowns (if the trip is terminated at Trondhjem, one hundred and eighty crowns), covering second class railway accommodations with sleeping cars, board and lodging, excursions, guides and tips; (*c*) Stockholm—Visby—Stockholm, air route; one day; price one hundred and fifty crowns, covering meals, automobile excursions on the island of Gotland, guides and tips.

Reservations should be made as soon as possible (not later than July 1), and be accompanied by a deposit of fifty crowns.

Below is a survey of travel routes from the terminal points of trips 8 *a* and *b*: from Gothenburg to Trälleborg and Sassnitz, to London, to Antwerp, to Malmö and London, and to Antwerp; from Trondhjem to Stockholm, Trälleborg and Sassnitz, to Oslo, Gothenburg, Trälleborg and Sassnitz, to Oslo, Gothenburg, Rotterdam and Antwerp, to Bergen, Newcastle and Rotterdam, and to Oslo and Antwerp.

The Swedish State Railways Travel Bureau has the following branch offices:

London W 1, Swedish Travel Bureau, 21 Coventry Street. Telegraphic address: Suedecus.

New York, Swedish State Railways Travel Information Bureau, 551 Fifth Avenue. Telegraphic address: Swedtravel.

Paris, Chemins de fer de l'État de Suède, Bureau de voyages, 5, Avenue de l'Opéra. Telegraphic address: Suedecus.

Berlin W 8, Schwedisches Reisebureau, Unter den Linden 22—23. Telegraphic address: Suedecus.

Amsterdam, Officieel Reisbureau der Zweedsche Staatsspoorwegen Louis Hannell, Visschersdam 7. Telegraphic address: Hannellreis.

Copenhagen, Sveriges Statsbanors Sovplatscentral, Hovedbanegaarden. Telegraphic address: Sovecent.

Persons desiring to remain in Sweden for part of the summer of 1930 are advised to consult a traveler's bureau, and to order through the bureau or through the Swedish organization committee, a copy of the booklet called "Summer in Sweden," printed in English and edited by the Swedish Traffic Association (Svenska Trafikförbundet) Stockholm. This booket contains brief, clear information, with maps on watering places, resorts and summer sports in Sweden.

All communications are to be addressed to *The Second International Pediatric Congress, Stockholm, Sweden.* Telegraphic address: *Pediatric, Stockholm.*

Applications for tickets of admission should preferably be accompanied by the fee, sent as a check or a money order.

For the avoidance of errors, it is absolutely necessary that all names and addresses be written with printed characters or typewritten.

Further announcements will appear later on.

Stockholm, January, 1930.

I. JUNDELL, M.D.,
Chairman, Swedish organization committee.

NILS MALMBERG, M.D.,
Secretary, Swedish organization committee.

GENERAL

Infant Mortality in Holland.—According to official statistics, the mortality rate for 1928 was 9.61 per one thousand inhabitants; this rate is 0.63 less than that for 1927 and is also the lowest recorded. This decrease in mortality is partly due to a decrease in infant mortality, which is larger in the country than in the towns. In 1880-1884 the infant mortality was 19.09 per hundred children born alive; in 1900-1904 it was 14.12, and in 1920-1923, 6.83; in 1927 it decreased to 5.87, and in 1928 to 5.23. Almost every year the highest mortality occurs in the hot summer months. The number of deaths from diarrhea and enteritis in children under the age of 2 years is decreasing in a high degree: Between 1911 and 1915 the mortality rate for boys was 10.7 per ten thousand and for girls, 7.80; in 1921-1923, it was 4.31 for boys and 3.14 for girls, and in 1928, 1.54 for boys and 1.10 for girls. In 1911-1915, congenital debility and malformations caused a mortality of 5.89 per ten thousand in boys and 4.33 in girls; in 1921-1923, 3.41 in boys and 2.45 in girls, and in 1928, 5.65 in boys and 3.94 in girls.

The mortality from infectious diseases decreased to a high degree after 1870. From 1840 to 1849, there were 4.79 stillbirths per hundred new-born and from 1920 to 1923, 3.78, this being the number of children who died before their births were registered officially. From 1924 to 1928 the number of really stillborn children was 2.55 per hundred new-born and in 1928, 2.51. Since 1924 the deaths in children less than 1 year of age include those in infants that were born alive, but died before their births were officially registered.

Raleigh Fitkin Memorial Pavilion Dedicated.—The Raleigh Fitkin Memorial Pavilion at the New Haven Hospital was dedicated on February 9. The pavilion was the gift of Abram E. Fitkin, New York, who gave $600,000 for the construction of the building, and $500,000 to establish an endowment for the work in children's diseases.

New Home for Destitute Crippled Children.—Ground was broken on Feb. 19 for the two units of the Home for Destitute Crippled Children at the University of Chicago. The buildings were made possible through the gifts of $300,000 each from Mrs. Gertrude Dunn Hicks and Mrs. Elizabeth McElwee. These buildings will be given over entirely to wards; the surgical and roentgen services are to be located in the Billings Hospital.

UNIVERSITY NEWS

The University of Pennsylvania and the Children's Hospital of Philadelphia have made an agreement for affiliation of the pediatric department of the School of Medicine with the medical division of the Children's Hospital.

By the terms of this agreement the professor of pediatrics in the School of Medicine will become physician-in-chief of the medical division of the Hospital, and the staff of the medical service will be composed of members of the pediatric faculty.

Dr. Frederic W. Schlutz, professor of pediatrics of the Medical School of the University of Minnesota has accepted the newly established chair of pediatrics at the Medical School of the Ogden School of Science of the University of Chicago.

CORRECTIONS

In the article by Dr. Kutsuji Kato (Congenital Transposition of Cardiac Vessels: A Clinical and Pathologic Study, Am. J. Dis. Child. **39**:363 [Feb.] 1930) footnote 2 is incomplete. It should read:

"2. There seems to be confusion on the part of the author who prints an autopsy picture of a case of complete visceral dextroposition describing it as a case of complete transposition of cardiac vessels. See Griffith, J. P. C., and Mitchell, A. G.: The Diseases of Infants and Children, ed. 2, Philadelphia, W. B. Saunders Company, 1926, vol. 2, p. 381."

In the article by L. T. Royster, M.D., and C. N. Hulvey, M.S., LL.B., entitled, "The Relations of Weight, Height and Age in Negro Children" (AMERICAN JOURNAL OF DISEASES OF CHILDREN **38**:1222 [Dec.] 1929), the headings for the third and fourth columns in tables 4 and 5 were given incorrectly. These should read:

Height in Inches	Height in Inches
Colored (R and H)	White (B and W)

Abstracts from Current Literature

Anatomy and Physiology

HETEROGENOUS EPITHELIUM IN THE OVARIES OF CHILDREN. S. AKAGI, Arch. f. Gynäk. **134**:390, 1928.

Numerous ovaries of children were examined and several small cystic epithelial formations consisting of ciliated cylindric cells, mucus-producing goblet cells or squamous epithelial cells were observed. Only one type of epithelium was usually present in the individual cysts. In cysts lined by ciliated cells or goblet cells, ova were seen. But these cysts are not considered as derivatives of granulosa epithelium, but as results of specific congenital anlagen which were present in the granulosa layer of the ovum. The heterogenous epithelial cells of the ovary originate from corresponding congenital anlagen of Mueller's epithelium.

W. C. HUEPER.

THE POSSIBILITY OF MEASURING THE SELLA TURCICA IN CHILDHOOD. WALTER SARTORIUS, Monatschr. f. Kinderh. **45**:259 (Nov.) 1929.

With a certain modification of roentgen technic the writer has found that he can make accurate determinations of the size of the sella turcica in childhood.

GERSTLEY, Chicago.

Pathology, Bacteriology and Biochemistry

THE EFFECT OF ROENTGEN IRRADIATION ON THE VELOCITY OF ERYTHROCYTE SEDIMENTATION. E. H. RUBIN and OTTO GLASER, Am. J. Roentgenol. **18**:520 (Dec.) 1927.

The authors conclude that the increased erythrocyte sedimentation after irradiation was due to the heat generated during the process of roentgen radiation by unfiltered rays. The increased velocity of erythrocyte sedimentation is due to increased temperature and is probably caused by changes in the plasma rather than in the red cells.

STULIK, Chicago.

THE CARBON DIOXIDE DISSOCIATION CURVE OF THE BLOOD IN INFANCY AND CHILDHOOD. NOAH MORRIS and STANLEY GRAHAM, Arch. Dis. Childhood **4**:299 (Oct.) 1929.

The limits of the carbon dioxide dissociation curves obtained from the blood of ten normal children at 40 mm. of mercury ranged from 47 to 56 volumes per hundred cubic centimeters.

PETERMAN, Milwaukee.

CAROTINEMIA AND PLASMATIC XANTHOCHROME. N. FIESSINGER, H. WALTER and J. E. THIERRY, Compt. rend. Soc. de biol. **98**:1297 (May 18) 1928.

The color of the serum is an indication of the degree of cholemia, bilirubin being the only constituent which colors it. The simplicity and rapidity of methods based on this fact make them useful in practice, though subject to error, for determining the biliary plasmatic index. Carotine pigments, when abundant in food (carrots, oranges), upset the method by direct estimation mentioned, especially when oxidations are slow, but in normal and ordinary hepatic pathologic conditions the carotinemia does not affect the value of the method in determining bilirubin retention.

KUGELMASS, New York.

INFLUENCE OF ULTRAVIOLET RAYS AND OF VIOSTEROL ON THE SERUM OF NORMAL BLOOD. G. FRONTALI, Riv. di clin. pediat. **27**:699 (Sept.) 1929.

Ultraviolet irradiation of blood serum increases its organic phosphorus content. The increase also occurs in blood serum freed of its protein and lipoid. Thus it appears that the added inorganic phosphorus is derived from acid-soluble organic phosphorus.

Viosterol and irradiated olive oil similarly increase the inorganic phosphorus of blood serum "in vitro."

HIGGINS, Boston.

EXPERIMENTAL TETANY CATARACT. H. GOLDMANN, Arch. f. Ophth. **122**:146 (May) 1929.

The author made extensive and careful slit-lamp studies on animals after experimental removal of the parathyroid glands. In rats and in dogs, opacities of the lens occurred only if muscular symptoms of tetany were present. If the muscular symptoms were avoided (calcium lacticum by mouth), the lenses remained normal. Hyperemia of the anterior ciliary vessels seemed to favor the development of opacities of the lens. Miotics and mydriatics had no definite influence. In rats an intimate connection between the attacks of convulsions and the appearance of opacities in the lens could be observed. After the first attack, fine gray points appeared immediately beneath the anterior capsule of the lens. If all further attacks were avoided, most of the fine opacities disappeared, while moving a little toward the center of the lens. If further muscular attacks were allowed to take place, the primary gray dots developed into gray vacuoles. These vacuoles were small in the axial parts of the lens and became larger toward the periphery. The vacuoles grew and formed small tubes. The whole opaque layer gradually moved away from the surface of the lens. The fibers around the vacuoles were destroyed too. The slit-lamp picture of the tetany cataract in dogs was principally the same as that in rats. The opacities of the lens were interpreted as the reaction of the living lens fibers to an acute intoxication. The gray dots which occurred in rats and dogs as the first symptom of lesions of the lens were the opaque ends of lens fibers and not lesions of the epithelium, because they were found in the posterior subcapsular layer of the dog, which has no epithelium. The opaque layer always formed a new zone of discontinuity.

The clinical picture of the tetany cataract in rats was entirely different from that of the thallium cataract. Therefore, the author concluded, the thallium cataract had nothing to do with a lesion of the parathyroid glands.

The author was able to measure the growth of the lens by estimating the velocity with which the primarily subcapsular opacities divided down into the more central parts of the lens. It sometimes occurred that fibers which had been injured when they were near the surface became opaque when they had moved in a more central layer of the lens.

P. C. KRONFELD.

LYMPHOGRANULOMATOSIS OF THE MAMMARY GLAND. H. KÜCKENS, Beitr. z. path. Anat. u. z. allg. Pathol. **80**:135, 1928.

In a girl, aged 16 years, swelling of the right breast was noticed several weeks before operation. At this early stage the lesion was thought to be a tuberculous abscess secondary to tuberculosis of a rib. Progressive involvement of the entire breast and induration led to a later diagnosis of a malignant condition. The surgically removed tissue, when submitted to microscopic examination, was found to consist of characteristic Hodgkins granuloma, with eosinophils, plasma cells and Dorothy Reed-Sternberg giant cells. Most of the glandular tissue had been replaced by the granulation tissue. The latter had diffusely invaded the underlying pectoral muscle and had extended to the left of the midline. No involvement of any lymph node group could be detected on later careful examination, and the author considers the case one of primary localization of lymphogranulomatosis

in the mammary gland and the only case of this kind recorded in the literature. Kauffmann describes a case of axillary lymph node lymphogranulomatosis which involved the mammary gland and pectoral muscle by direct extension.

[ARCH. PATH.]

HISTOLOGY OF CHONDRODYSTROPHIC CHICK EMBRYOS. W. LANDAUER, Virchows Arch. f. path. Anat. **271**:534, 1929.

Histologic study of the endocrine organs of chondrodystrophic chicks, removed from the shell on the twenty-second day of incubation, failed to reveal any changes which might be correlated with the chondrodystrophic condition. The only change noted was somewhat delayed differentiation of all the endocrine organs, as compared with normal embryos of the same age.

[ARCH. PATH.]

TERATOMA OF THE HYPOPHYSEAL REGION WITH REFERENCE TO SUPRARENALS IN ANENCEPHALY. E. J. KRAUS, Virchows Arch. f. path. Anat. **271**:546, 1929.

An otherwise well formed prematurely born girl, 42 cm. long, had a teratoid tumor which protruded into the cavum cranii and into the pharynx; the canalis craniopharyngeus was wide. The brain was normal. The anterior lobe of hypophysis was found on the posterior aspect of the cranial part of the tumor; it was compressed but normal. Rathke's cysts and posterior lobe were absent. The suprarenal glands were normal. Therefore, one cannot assume that in anencephaly the defect of the suprarenal glands is due to absence of the posterior lobe of the hypophysis.

PLAUT, Chicago.

SENSITIVITY OF THE RED BLOOD CELLS TO LIGHT. W. MEYERSTEIN, Wien. Arch. f. inn. Med. **18**:359, 1929.

Light definitely influences the composition of the blood.

The longer wave-lengths of the red and infra-red portion of the solar spectrum penetrate tissue more deeply than do the shorter ultra-violet rays.

The longer wave-length rays can bring about hemolysis.

This photohemolysis of the erythrocyte may be beneficial to the organism in that the more rapid destruction of the red cell favors stimulation of blood regeneration.

SCHLUTZ, Minneapolis.

THE ULTRAFILTERABLE FRACTION OF SERUM CALCIUM. W. HERTZ, Ztschr. f. Kinderh. **47**:215, 1929.

A method has been worked out for the ultrafiltration of small quantities of serum. The sources of error have been thoroughly determined. The absolute value in infants and children was found to be between 4.4 and 5.0 mg. per hundred cubic centimeters. Up to this time, only normal values for adults and values in healed spasmophilia have been published.

EMERSON, Boston.

THE TECHNIC OF THE DETERMINATION OF BASAL METABOLISM IN INFANTS: I. DOES DIETHYL-DIALLYL-BARBITURATE OF DIETHYLAMINE INFLUENCE THE EXCHANGE? H. BAER, Ztschr. f. Kinderh. **47**:226, 1929.

In diethyl-diallyl-barbiturate of diethylamine a narcotic has been found for infants and small children which leaves the metabolism completely uninfluenced, and on the basis of this fact it has been possible to make accurate determinations.

EMERSON, Boston.

THE TECHNIC OF THE DETERMINATION OF BASAL METABOLISM IN INFANTS: II. THE QUESTION OF CONSTANCY OF THE VALUES OF BASAL METABOLISM IN BABIES. H. BAER, Ztschr. f. Kinderh. **47**:231, 1929.

The values for basal metabolism calculated by Kestner-Knipping, according to the Benedict-Harris table for adults, agree with Baer's which were actually determined. The height of the basal metabolism depends on the height of the caloric intake which an infant receives in the stage previous to the determination. Overfeeding causes in different conditions of nutrition wholly different results. Secondary specific dynamic activity is in general the greater, the less the need of the body for foodstuffs; it is greatest in eutrophia, less in hypotrophia and least in atrophia. In order to exclude this error, it was insisted that the infant be left for several days on a maintenance diet before the determination of the gas exchange. If, besides resting and fasting, this condition was fulfilled, the physiologic range of variation of the basal metabolism was analogous to that of adults, within the limits of plus or minus 6 to plus or minus 10 per cent of the standard values. On the basis of these results, it has been established that the basal metabolism value for the same mass is constant.

EMERSON, Boston.

GRAVIMETRIC METHOD FOR DETERMINATION OF IRON. G. SVEDENIUS, Acta paediat. **9**:1, 1929.

The iron is precipitated from an acid solution with nitroso-beta-naphthol. The precipitate is then collected, ashed in a platinum crucible, and weighed as ferric oxide on a microbalance. Copper and cobalt are also precipitated by the reagents used, but there is no carrying down of phosphates. In the author's hands, the method is accurate to about $\pm$ 0.04 mg.

MCINTOSH, Baltimore.

Nutrition

THE INFLUENCE OF CERTAIN VITAMIN DEFICIENCIES ON GASEOUS EXCHANGE IN CHICKS: I. RACHITIS. F. M. BALDWIN, V. E. NELSON and C. H. MCDONALD, Am. J. Physiol. **85**:348 (June) 1928.

Prolonged absence of vitamin D in the diet is marked by a definite fall in the respiratory quotient, which immediately precedes the symptoms of rickets. It is inferred that the antirachitic substance is essential for normal metabolism of the growing chick, especially for the utilization of carbohydrates.

KUGELMASS, New York.

I. ULTRA-VIOLET WAVE-LENGTHS RESPONSIBLE FOR CURE OF RICKETS IN CHICKENS. II. SOME PHASES IN THE TREATMENT OF RICKETS IN CHICKENS BY ULTRA-VIOLET RADIATIONS. G. H. MAUGHAN, Am. J. Physiol. **85**:392 (June) 1928.

1. The best wave length is 2,968 Angström units. 2. Feathers and clothing prevent the absorption of ultraviolet rays. Irradiated chicks, if treated daily, partially protect nonirradiated chicks from rickets when kept in pens with them.

KUGELMASS, New York.

RICKETS OCCURRING LATE IN CHRONIC INTERSTITIAL NEPHRITIS: REPORT OF A CASE. ROLLA G. KARSHNER, Am. J. Roentgenol. **18**:442 (Nov.) 1927.

Renal dwarfism, renal rickets, renal infantilism or rickets of adolescents is rarely mentioned in the literature. In 1883, Lucas mentioned the connection between late rickets and albuminuria. More recently, Barber defined renal dwarfism as a condition of stunted development associated with bone deformities of the late rickets type due to an insidious chronic interstitial nephritis of obscure etiology.

Three stages are described: (1) in young children, manifested by underdevelopment and thirst; (2) toward puberty, manifested by typical signs of renal dwarfism and late rickets; (3) in adolescence (exceptional), when the epiphyses actually join the shafts. Death usually occurs between the seventh and the seventeenth year. The differential diagnosis includes diabetes insipidus, bilateral cystic kidney and bilateral renal calculus. In five cases studied, low calcium rickets was present. In the case reported; a child with chronic interstitial nephritis exhibited clinically, pathologically and roentgenographically active rickets, with onset in infancy and persistence until death at 9 years of age in spite of an intense antirachitic regimen.

STULIK, Chicago.

OBSERVATIONS ON THE USE OF IRRADIATED ERGOSTEROL IN ACTIVE RICKETS. JACOB SOBEL and IRVING CLAMAN, Arch. Pediat. **46**:1 (Jan.) 1929.

The authors employed a 1 per cent solution of irradiated ergosterol in oil, two and one-half drops of which contained 1 mg. of viosterol (irradiated ergosterol), in the treatment for rickets at the Hospital for Joint Diseases. The study was limited to these cases which were controlled by clinical, laboratory and roentgen observations. The use of cod liver oil and actinotherapy was discontinued.

On admission observations were made on the weight, blood count, blood calcium and inorganic phosphorus, urinalysis and roentgenologic appearance of the long bones. Irradiated ergosterol, from 4 to 12 mg. daily, was given at the beginning of the studies; from 1 to 4 mg. was given later. No eggs were given.

The general condition of the patients improved markedly. They were happier and more animated, and their appetites improved. There was a rapid and progressive increase in weight. There was no change in temperature attributable to the irradiated ergosterol.

The effect on craniotabes was marked, sometimes dramatic, the condition clearing up in two weeks in some instances.

The closure of the anterior fontanel did not keep pace with the response of craniotabes. The authors believe that the fontanel closes early in spite of active rickets and that the fontanels of children, sick or well, close earlier than they did in former years. Beginning calcification at the wrist epiphyseal line was observed within two weeks, marked calcification in four weeks. Cupping or fraying usually disappeared in eight weeks.

The rachitic rosary is one of the last signs to yield. It did not seem to disappear within the period of observation — from five weeks to three months.

Not all cases showed the symptom of sweating; one case cleared up within two months.

The blood calcium content was from 9.5 to 11.6 mg. per hundred cubic centimeters of whole blood. This is more or less the rule in rickets. The inorganic phosphorus reached normal limits (from 5.4 to 6.9 mg.) in from one to ten weeks. Hypercalcemia was not observed. The blood calcium content in all the patients was normal, probably because most of them were in the second year of life (from 11 months to 2½ years).

The authors express their belief that from 3 to 4 mg. (from eight to ten drops) of vigantol daily is the optimal dose for children over 1 year of age (five drops of vigantol equals 2 mg. of irradiated ergosterol). This is divided into two or three equal doses daily. The daily dosage is regulated by the degree of activity of the disease. In children under 1 year of age, from 1 to 2 mg. (from three to five drops) daily are given; in premature infants and as a preventive, from 1 to 2 drops daily (from 2.5 to 4.5 mg.). After from three to six weeks, a check-up is done serologically and roentgenologically, and the preparation may be discontinued or the dosage reduced. No ill effects were noted when as much as 12 mg. (thirty drops) was given daily for twenty days. There was no disturbance of kidney function. The authors confirm the observations of others as to the effect of the preparation and believe it will supplant cod liver oil and irradiation of the skin.

WILSON, Norfolk, Va.

THE RELATION OF FOOD TO TEETH IN CHILDREN. FLOYD CLARKE, Nebraska M. J. **14**:439 (Nov.) 1929.

The author stresses the cooperation between the dentist and the physician. Prenatal influences are less important than postnatal. Mixed diets containing foods rich in vitamin D are recommended. Calcium and phosphorus are necessary, as is sunlight or quartz light.

HAMILTON, Omaha.

THE EXAMINATION OF IRRADIATED ZYMOSTEROL FOR THE PRESENCE OF VITAMIN D. E. M. HUME, H. H. SMITH and I. SMEDLEY-MACLEAN, Biochem. J. **22**:980, 1928.

The experiments were carried out on rats, using four different diets and different criteria of healing or prevention of imperfect calcification: (1) For a diet deficient solely in vitamin A and D, or (2) containing A through the addition of 20 per cent of wheat germ, the criterion was the percentage of ash of dried fat-extracted leg bones; (3) for diet 3,143 of McCollum, the criterion was the percentage of ash and the macroscopic examination of the rib junctions; (4) for diet 84 of Sherman and Pappenheimer, the criterion was x-ray pictures of the bones of the right leg and ash. The zymosterol used contained 5 or 12 per cent of ergosterol estimated from the amount of ultraviolet absorption; it was dissolved in hardened cotton-seed oil for administration to the rats. The p_H of the feces was estimated colorimetrically; bromthymol blue or phenol red was used. With the two complete diets there was little difference in the reaction of the feces between the controls and the experimental animals; with the other two diets the controls had alkaline feces, and the animals given oils less alkaline provided the dose was large enough. The complete diets failed to show whether the effect produced by irradiated zymosterol was due to ergosterol present in it or not; $\frac{1}{4 \times 10^6}$ mg. of irradiated ergosterol improved the ash content of the bones. With the two deficient diets it was possible to show that the effect produced by irradiated zymosterol was due solely to its content of ergosterol. Hence, zymosterol is not activated by irradiation.

KUGELMASS, New York.

VITAMIN A FORMATION: THE FEEDING OF ETIOLATED WHEAT SHOOTS TO RATS KEPT IN DARKNESS. T. MOORE, Biochem. J. **22**:1097, 1928.

The rats were kept in a dark room illuminated by a ruby light, and the shoots were exposed to this light for as short a time as possible. From fifteen to thirty shoots daily produced resumption of growth in animals depleted of vitamin A on a diet free from this vitamin but containing B and D. Thirty wheat seeds daily were without influence. Fairly good growth was obtained on fifteen shoots daily fed from the commencement of the experiment, when the diet was also free from D. Hence, vitamin A is formed in etiolated wheat shoots in the dark, or possibly under the influence of red light. Long exposure to red light will result in the synthesis of chlorophyll.

KUGELMASS, New York.

FEEDING IN SEVERE STATES OF MALNUTRITION: THE CASE OF AN INFANT FED ON THE PUDDING DESCRIBED BY MOLL. JEAN CATHALA and IDI BITSCH, Bull. Soc. de pediat. Paris **27**:199 (April 19) 1929.

The authors used the pudding diet described by Moll and Stransky, which contains flour, sugar, butter and a whole egg mixed with water and baked in a double boiler for at least an hour and a half and then diluted with water (slightly sweetened tea). They fed this diet to an athreptic infant who thrived on it. They point out, however, that the infant had already begun to improve when it was started on this diet and would doubtlessly have recovered without it. They wish merely to draw attention to the fact that the infant tolerated the diet, and that such a diet can be used although it has no other value than that of a rich high-caloric feeding.

BENJAMIN, Montreal.

THE ANTIRACHITIC ACTION OF IRRADIATED "HÉLISTÉRINE." G. MOURIQUAND and A. LEULIER, Presse méd. **37**:1261 (Sept. 28) 1929.

The authors have given the name "Hélistérine" to a mixture of cholesterol and irradiated cholesterol lipoids of *Helix pomatia* (snail). This animal product has exactly the same action as the inorganic cholesterol from ergot. The antirachitic potency of hélistérine is such that one drop equivalent to $\frac{1}{50.000}$ Gm. of the mixture is sufficient to protect the ordinary sized rat from rickets. This product should therefore be of value in protecting infants from rickets.

SANFORD, Chicago.

EXPERIMENTAL STUDY OF THE COMPOSITION OF SOME ANIMAL MILKS, WITH SPECIAL ATTENTION TO THE NITROGENOUS SUBSTANCES. A. VENUTI, Riv. di clin. pediat. **27**:643 (Sept.) 1929.

Study of the composition of certain animal milks yielded the following percentages:

	Cow's Milk (4 Samples), Per Cent	Goat's Milk (10 Samples), Per Cent	Sheep's Milk (10 Samples), Per Cent	Ass's Milk (8 Samples), Per Cent
Total nitrogen	0.560	0.551	0.909	0.322
Nonprotein nitrogen	0.053	0.046	0.061	0.039
Protein nitrogen	0.512	0.505	0.847	0.283
Protein	3.26	3.21	5.39	1.80
Casein	2.74	2.59	4.54	1.20
Albumin	0.51	0.61	0.85	0.60
Fat	3.6	4.4	6.9	1.3
Lactose	4.85	3.92	4.33	5.80

HIGGINS, Boston.

VITOPHOS, A PHOSPHOROVITAMIN AGENT. MARTINEZ VARGAS, Med. de los niños **30**:225 (Aug.) 1929.

Vitophos is a vegetable compound containing an abundance of vitamins, in addition to assimilable phosphorus and calcium and magnesium salts. Vitamins A, B, D and E are present in sufficient quantities. It was found superior to all other forms of medication in rickets. It is also a useful agent in convalescence from a long debilitating illness, in grave anemias, some forms of tuberculosis, cardiopathies, arteriosclerosis and in certain cases of cancer and diabetes in which there is disturbed nutrition.

DWYER, Kansas City, Mo.

THE CHANGES IN THE HYPOPHYSIS FROM VITAMIN B DEFICIENCY. S. A. SATWORNITZKAJA and W. S. SIMNITZKY, Virchows Arch. f. path. Anat. **269**:54, 1928.

In the hypophysis of pigeons, droplets of albuminous material appeared in the protoplasm of the basophilic cells most marked on the twenty-fifth day of disease. After twenty-five days, the vacuolization usually regresses, and transitions from the vacuolated to the normal cell types appear in the glands. At the same time, vacuoles appear in the eosinophilic cells, but these vacuoles could not be stained with any of many methods tried. The intralobular colloid becomes less in amount and may disappear almost completely; toward the end of the condition it reaccumulates but never to the extent present in the normal gland. The appearance of vacuoles in the cells indicates that there is an increased function related to the carbohydrate metabolism in this disease. The changes are more marked in the male than in the female pigeons and are greater in spring and summer than in winter. In rats the basophils of the hypophysis seem to be increased and the eosinophils diminished. Qualitative changes in the cells are much less in degree

since the symptoms of vitamin B deficiency in rats take a long time in appearing; whatever changes there are in the hypophysis of rats are related to the carbohydrate metabolism. The necrobiotic changes in the cells of both pigeons and rats are not characteristic and are probably due to changes in the nutrition.

[ARCH. PATH.]

Prenatal Conditions

CERVICAL RIB. JAMES MAXWELL, Proc. Roy. Soc. Med. **22**:1240 (July) 1929.

A case of cervical rib was reported in a girl, aged 5 years.

WILLIAMSON, New Orleans.

SPINA BIFIDA. JOHN FRASER, Edinburgh M. J. **36**:284 (May) 1929.

Fraser expresses his belief that there will continue to be interest in the correction of spina bifida even if there are opinions in the profession that surgical efforts are largely wasted. He predicts that in one hundred years spina bifida will be discussed from the preventive standpoint through knowledge acquired from experimental embryology. In discussing the explanation of this maldevelopment, the theories of which are not yet sufficient, he mentions the fact that spina bifida has been produced experimentally in the chick. He quotes Richter's observation that this condition develops in 6 per cent of chickens when the temperature of the egg is varied. The theory that seems most plausible, Fraser believes, is the one offered by Mall, His and Ballantyne, that one must lay the initial blame on the decidua rather than on the ovum. There is probably an interference with the proper source of nourishment, and not any mysterious primary derangement of the embryonic cells.

This paper contains numerous photomicrographs which illustrate the arrest in development which produces spina bifida. Illustrations of transverse sections show the structure of meningocele, myelomeningocele, and spina bifida occulta. Sections of the sac wall and neural tissue of the cord are shown. The clinical examination is made more scientific by the method of oxygen injection before taking the x-ray picture. An apparatus is shown which was introduced at the Edinburgh Children's Hospital by Mr. Norman Dott, for the purpose of replacing spinal fluid with sufficient gas so that the relation of the parts inside the sac may be outlined by the roentgen rays.

The only line of treatment is the operative removal of the sac, the attempt to restore the nerve tissue to an approximately normal condition, and the repair of the congenital defect in the muscle and bone. The success of operation depends: (1) on selection of suitable cases, as determined by the child's age, type of spina bifida, condition of tumor wall, coexistence of paralysis, general condition of the child, and hydrocephalus. Operative procedure is relatively simple in the type of spinal meningocele. Operative technic is graphically illustrated.

Results of treatment at the Edinburgh Sick Children's Hospital, in 130 suitable cases of 191 presented during twenty-five years, show that 82 children lived to be discharged with the wound healed and the cleft removed; 48 of these died of a secondary condition, and 30 lived but most of them were crippled in mind and body. At present, therefore, one is tempted to doubt the value of attempting treatment.

NEFF, Kansas City, Mo.

CONGENITAL ANOMALIES OF THE FORAMEN SPINOSUM. DAVID M. GREIG, Edinburgh M. J. **36**:363 (June) 1929.

Greig states that congenital anomalies of the foramen spinosum alone occur occasionally. He describes two skulls in which the main trunk of the middle meningeal artery was deficient; in one skull the right foramen was extremely small and unlike an arterial foramen, while in the other skull the right foramen

was absent. The original defect was of the artery and not of the foramen, probably because this artery has such a complicated development. The history of the patients is unknown except that one was a girl, aged 18 years, who had congenital mental deficiency. Greig does not say whether he thinks the arterial abnormality produced the mental deficiency.

NEFF, Kansas City, Mo.

REEXAMINATION OF PREMATURE INFANTS. S. RANKE, Acta Paediat. **9**:46, 1929.

This is a report of 155 infants, whose birth weight was 2,500 Gm. (5½ pounds) or less, who were cared for at the Flensburg Children's Hospital at Malmö in the period 1915-1924 and who could be followed by examination or questionnaire. All the survivors reported on were over 3 years of age. The number that died during their first year of life constituted 87.5 per cent of the group with a birth weight of less than 1,000 Gm. (2 pounds, 3 ounces); 64 per cent in the group weighing from 1,000 to 1,500 Gm.; 55 per cent in the group weighing from 1,500 to 2,000 Gm., and 34 per cent in the group weighing from 2,000 to 2,500 Gm. In the whole series the mortality was 52.9 per cent. The incidence of mental deficiency was 5.5 per cent of the survivors; no cases of Little's disease, however, were found. Weights and measurements indicated that these children as a whole were underweight for their height, and it was the author's impression that the incidence of neuropathic subjects was high.

MCINTOSH, Baltimore.

Diseases of the New-Born

EPIDEMIC PEMPHIGUS OF THE NEWLY BORN. FRANK C. NEFF, Arch. Pediat. **46**:24 (Jan.) 1929.

The disease appears to be very common in lying-in hospitals. It seems to have no seasonal incidence but is favored by moisture and warmth. Sixty-five cases are reported from the Kansas City General Hospital. The spreading depends on the lack of aseptic precautions. The lesions first appear on the third to the eleventh day, usually on the sixth. There was no elevation of temperature in the series observed, except in a fatal case with sepsis. The duration is from a few days to several weeks and spreads by auto-inoculation. Local treatment seems to be of little or no value. The weight and general well being of the patients are usually not affected. Bacteriologic studies suggest *Staphylococcus aureus* as the causative organism; other organisms appear to be secondary invaders. *Streptococcus* in pure culture has been found in a primary lesion. Consideration of the source of the causative organism is speculative only. Poor aseptic precautions are often responsible for the spread of the disease.

The course is self-limited; ammoniated mercury ointment, mercurochrome-220 soluble or gentian violet is without proved effect. The author has used Milian's alcoholic solution of brilliant green and crystal violet with apparently curative effect but warns against too great enthusiasm. Prophylaxis and isolation are stressed.

WILSON, Norfolk, Va.

HELP BY THE MOTHER DURING LABOR, CAUSING DEATH OF THE CHILD. W. H. SCHULTZE, Deutsche Ztschr. f. d. ges. gerichtl. Med. **13**:21, 1929.

Difficulty in explaining the injuries and death of a newly born child finally resulted in tracing them to an arm presentation and self-delivery by the unwed mother when she was alone. The swollen left hand, the direction and location of abrasions and nail scratches corroborated the story told by the mother. A fracture of the cranium and an injury of the brain occurred by pressure of the head in the birth canal, when the child was born "conduplicato corpore." The self-aid was successful because the woman was a multipara and labor was several weeks early; the weight of the child was only 1,700 Gm. The child was born alive and lived about two hours. For a time, the mother was suspected of infanticide.

LE COUNT, Chicago.

POSTMORTEM EXAMINATION OF THE HEAD OF NEW-BORN. ERIK RYDBERG, Acta path. et microbiol. Scandinav. **6**:145, 1929.

The bones of the cranial vault are carefully separated from the parietal dura, and removed piecemeal. The dura is then examined and removed sufficiently so that the brain can be taken out in the usual way, except that the brain-stem is cut across, so that the tentorium and the contents of the posterior fossae can be examined thoroughly. The advantages of the method are that extravasations of blood over the surface of the brain can be studied satisfactorily in situ without the mixture of blood set free during the opening of the skull; the veins that open into the longitudinal sinus can be followed easily; the tentorium can be examined in situ, and the brain removed without damage. The disadvantage of the method lies in the fact that the bones of the vault are removed piecemeal; hence successful restoration of the head is rather difficult.

[ARCH. PATH.]

Acute Infections

RELATION OF VARICELLA TO HERPES ZOSTER. T. M. RIVERS and L. A. ELDRIDGE, JR., J. Exper. Med. **49**:899 and 907, 1929.

Varicella most frequently occurs in persons under 10 years of age, while zoster as a rule is observed in persons beyond that age. The number of cases of varicella exhibits a markedly constant seasonal variation. The variations in the prevalence of herpes zoster are not regular and do not parallel those of varicella. Experiments and clinical observations dealing with the identity of the viruses of varicella and herpes zoster are presented. The results indicate that the etiologic agents concerned with these two diseases are in the majority of instances not identical.

AUTHORS' SUMMARY [ARCH. PATH.]

INTRADERMAL VERSUS SUBCUTANEOUS IMMUNIZATION OF MONKEYS AGAINST POLIOMYELITIS. F. W. STEWART and C. P. RHOADS, J. Exper. Med. **49**: 959, 1929.

The introduction of considerable amounts of living, active poliomyelitis virus into the skin and subcutaneous tissue of monkeys protects the animals against intracerebral inoculations of similar virus material. The degree of protection conferred by intradermal is greater than that by subcutaneous injection. During intradermal and subcutaneous inoculations, no local or general pathologic signs were observed. The degree of protection produced by the immunization methods used is not absolute, since a percentage of the inoculated monkeys respond to intracerebral injections of highly potent virus. The serums of the animals inoculated intradermally or subcutaneously neutralized poliomyelitis virus in vitro, irrespective of the result of intracerebral inoculation, in all except one instance. The power of the serum of treated monkeys to neutralize virus in vitro is a more delicate test of immunity than is the intracerebral inoculation.

AUTHORS' SUMMARY [ARCH. PATH.]

A STUDY OF THE SIGNIFICANCE OF GEOGRAPHIC AND SEASONAL VARIATIONS IN THE INCIDENCE OF POLIOMYELITIS. W. LLOYD AYCOCK, J. Prev. Med. **3**:245, 1929.

There is evidence that, in man, infection with the virus of poliomyelitis manifests itself in different ways; frank disease in relatively few and immunization without recognizable disease in the majority. Data presented in this paper indicate that these different reactions to infection with the virus may be due to variations in the physiology of the host, rather than to variations in the virus. Intracerebral inoculation of the virus in monkeys uniformly produces fatal poliomyelitis, and repeated intracutaneous inoculation of active virus produces immunity without symptoms of

the disease, but neither of these methods reproduces an attack of the same degree of severity as that seen in man. It was found, however, that intranasal instillation of the virus reproduces poliomyelitis of nearly the same order of severity as that observed in man. The disease developed in only a portion of the animals following intranasal instillation of the virus, and — what seemed to be more significant — in many of the animals a much milder form developed than that which practically always follows intracerebral inoculation. Furthermore, in one instance in which the animal showed no symptoms following intranasal inoculation, its blood serum in three separate tests was found to be capable of neutralizing the virus. From this, it appears that monkeys may possess a resistance to intranasal instillation of the virus not unlike that which man possesses to infection by natural means. It may be possible, therefore, to gain further knowledge of this form of resistance to poliomyelitis (autarcesis) by testing the influence of artificial alterations in physiologic functions of the monkey on the results of intranasal instillation of the virus.

AUTHOR'S SUMMARY [ARCH. PATH.]

CONGENITAL MALARIA. LAFFONT, BINET and LESINI, Nourrisson **17**:295 (Sept.) 1929.

The mother of the patient here reported had had attacks of malaria since the age of 5 years. Two days before her confinement she developed chills and fever. The infant was born by breech extraction without difficulty, weighed 4,050 Gm. and was apparently in excellent condition. When 12 hours old the infant developed a fever which promptly disappeared after injections of quinine.

Mother and infant were discharged on the ninth day; both were in good condition. The infant soon developed a fever and died in three days. The diagnosis of congenital malaria is based on finding the plasmodia of tertian malaria in the smears made from the cord blood. The authors recommend that in similar cases the mother should be treated for malaria during the pregnancy, and the infant should receive antimalarial treatments beginning soon after birth.

McCLELLAND, Cleveland.

Chronic Infections

CHRONIC ADHESIVE PERICARDITIS IN CHILDHOOD. EVELYN HOLT, Am. J. M. Sc. **178**:615 (Nov.) 1929.

From a study of pericarditis in fifty children with rheumatic heart disease the author concludes that rheumatic pericarditis appears in association with severe infection and one which appears early in life, and that the prognosis is poor in that more than 33 per cent of those children who recover from the acute attack are likely to die within three years, probably 50 per cent will die within five years and few will ever lead a normal life. The author states that pericarditis is associated with valvular disease, usually with mitral stenosis, often with aortic insufficiency and is usually one part of a progressive heart disease.

Ascites appears as part of the general breakdown. When present, it presents a somewhat different picture than that described as Pick's disease.

HENSKE, Omaha.

A STUDY OF CHILDREN DISCHARGED FROM THE PRENDERGAST PREVENTORIUM. JOHN B. HAWES, JR., Am. Rev. Tuberc. **20**:41 (July) 1929.

The ultimate success of preventorium treatment depends on thorough, aggressive and prolonged follow-up work. No child should ever be allowed to return to a home where it will again be exposed to tuberculosis. Requirements for admission should be definitely lived up to. There must be a definitely positive von Pirquet test, definite and real contact, and detailed and adequate records of the child's social and medical history. Mental capacity as well as physical defects

should be investigated. To spend months of painstaking and detailed care of a child who will never get beyond a grammar school education is not promoting eugenics or raising the standard of citizenship to any great extent. Also, in order to preserve the family's self-respect and to help in preventing the abuse of medical charity, every family should be allowed, and indeed made, to pay something no matter how little for the care of the child while it is at the preventorium.

SMITH, Ogden, Utah.

A NEW ANALYSIS OF THE VALUE AND SAFETY OF PROTECTIVE IMMUNIZATION WITH B.C.G. (BACILLUS CALMETTE-GUÉRIN). S. A. PETROFF, Am. Rev. Tuberc. **20**:275 (Sept.) 1929.

The author challenges the statements of Calmette as to the value and safety of his method of immunization, and declares that after a careful consideration of the facts, there is little if any basis to support his claims. He analyzes the statistics offered by Calmette and the proponents of immunization with B.C.G., and concludes that they are open to severe criticism, and are so sprinkled with grave errors as to render them of no scientific value.

Petroff's own investigations have been made with four cultures of B.C.G. obtained at different times, which in general he has not found pathologic to a great extent. Lesions develop in experimental animals, but in the majority of cases completely disappear. In a small number of animals, progressive tuberculosis has been seen, leading to death, the lesions of which could be reinoculated with the same results. The virulence of the micro-organisms may sometimes be increased: (1) by rapid passage through animals; (2) by inoculating animals subcutaneously, followed by a second inoculation in a month or six weeks; (3) by cultivation on alkaline buffered synthetic fluid medium for a long time, subculturing at intervals of two weeks; (4) by cultivating in a medium containing 10 per cent antiserums, and (5) by dissociation. He claims to have isolated two types of organisms having different cultural characteristics; one of these is nonpathogenic and the other produces progressive disease in animals.

Recent studies on the biology of the tubercle bacillus suggests strongly that it is not stable and may show mutation. Although the B.C.G. is of relatively low virulence, it is possible that as it passes from human being to human being it may gradually regain its alleged greater former virulence. Infants that become infected with a virulent micro-organism and develop latent tuberculosis, may manifest a clinical disease later in life. At present there is not an iota of scientific evidence to show that the same thing may not occur if infants are infected with B.C.G.; there is accredited evidence to suggest that such a catastrophe might happen. A low level of acquired resistance is all that one can expect by the implantation of living micro-organisms. If a vaccine must be used, one composed of dead organisms can accomplish as much as B.C.G.

SMITH, Ogden, Utah.

ORAL VACCINATION WITH B.C.G. ON HUMAN BEINGS IN NEW YORK CITY. CAMILLE KERESZTURI, Am. Rev. Tuberc. **20**:297 (Sept.) 1929.

This is a report from the New York City Department of Health of a group of infants from tuberculous families, of whom 183 were given B.C.G. and 280 were used as controls. Of the vaccinated infants, 87 are now over 12 months of age. Slightly less than one half of the vaccinated infants with familial exposure have been separated from the family for one month or more.

The procedure is simple. The only difficulty encountered was with infants who had a tendency to regurgitation. The administration of the vaccine did not in any case cause elevation of temperature or other observable reactions. The tuberculosis mortality for this group was 1.2 for vaccinated and 8.6 for nonvaccinated controls. Of the two vaccinated infants who died of tuberculosis, one who lived in close contact with a father having positive sputum died of miliary

tuberculosis following whooping cough. Tubercle bacilli of the human type were demonstrated as the cause of this infection. The other infant died of miliary tuberculosis at the age of 4 months. This probably was a case of intra-uterine infection as the mother died of miliary tuberculosis shortly following her confinement. In seven cases in which definite data could be obtained, it was found that the bacilli were excreted with the stool between the eight and thirty-first hours after ingestion.

The subcutaneous or intracutaneous method of vaccination with B.C.G. is probably superior to the oral for the following reasons: The dosage is more certain; hypersensitiveness is obtained in almost 100 per cent of cases, and such vaccination need not be limited to the new-born. The authors conclude that oral administration of B.C.G. is relatively simple, is harmless and gives some degree of immunity the degree and duration of which cannot yet be determined.

SMITH, Ogden, Utah.

HEALED PULMONARY TUBERCULOSIS. T. M. LING, Proc. Roy. Soc. Med. **22**:1361 (Aug.) 1929.

In 1925, the patient, a girl aged 2 years, with a family history of tuberculosis, was treated four months previous to admission to the hospital for empyema. On admission she showed signs of incomplete left pneumothorax and bronchopneumonia over the left side. A roentgenogram showed the heart displaced to the right. The right side of the chest showed much discrete mottling, tuberculous in type, and a fibrosis of the base of the left lung, with a localized pneumothorax. The pneumothorax was subsequently tapped. On discharge, a roentgenogram showed large pneumothorax in the left side of the chest and collapse of the lung; in the right side of the chest the lung showed active infection. The patient was taken out of the hospital by her parents; twelve months later, she had gained 2 pounds (907 Gm.), and the general condition was good. At this stage, a roentgenogram showed much diffuse mottling at the base of the right lung (tuberculous). The left lung showed disease near the hilum, but no pneumothorax. At the time of report, a roentgenogram showed bilateral bronchiectasis which was rather more marked at the base of the right lung. The physical signs were in agreement with this observation.

WILLIAMSON, New Orleans.

THE FATE OF YOUNG CHILDREN IN TUBERCULOUS HOUSEHOLDS. G. LISSANT COX, and others, Tubercle **10**:497 (Aug.) 1929.

This comprehensive investigation, made by the tuberculosis officers of Lancashire, England, covered a district embracing a population of over 5,000,000. The histories of 1,486 children under 5 years of age, living in 1,063 homes, in each of which there were one or more cases of tuberculosis, were carefully analyzed. For purposes of comparison, the ordinary population of the geographic county of Lancaster was used as a control, as it nearly corresponded with the area in which the research was made.

Among the most significant conclusions resulting from this investigation were the following: Compared with the general population the death rate from nonpulmonary tuberculosis in children exposed to adults with positive sputum, was nine times greater in the age group from 0 to 1; fourteen times greater in the group from 1 to 2 years, and nineteen times greater in that from 2 to 5 years. This was mainly due to tubercular meningitis, which accounted for two thirds of the mortality. In children exposed to tuberculous adults with negative sputum, the nonpulmonary deaths were three times greater in the age group from 0 to 1; four times greater from 1 to 2, and ten times greater from 2 to 5, than among controls. The deaths from pulmonary tuberculosis were too few on which to base any conclusions. The death rate from causes other than tuberculosis during the first two years of life was appreciably less for exposed children than for the general population. From 2 to 5 years, however, the position was reversed.

With regard to the death rate from all causes, it was found that in the first year of life the children of tuberculous households had a death rate significantly below that of the general population, and for the second year; about the same as the latter. This lower mortality may be attributed to the special medical and nursing supervision to which tuberculous households are subjected.

The calculations made by Calmette, that in France 24 per cent of children of tuberculous mothers, not separated, die of tuberculosis in the first year, is many times higher than was found in Lancashire. This research shows that the death rate from tuberculosis for children of the corresponding group in this region was 3.2 per cent; from all causes the rate was only 11.5 per cent. The death rate from tuberculosis and from all causes for children observed from birth to 4 years, was a little lower than the French figures for children from 1 month to 4 years of age, vaccinated with B.C.G., and much lower than for the French children not vaccinated.

SMITH, Ogden, Utah.

THE DIAGNOSIS OF INTRATHORACIC TUBERCULOSIS IN CHILDREN. BERNARD SCHLESINGER, Tubercle **11**:1 (Oct.) 1929.

Perhaps the most valuable lesson that is to be learned at a children's hospital in regard to pulmonary tuberculosis is the unexpectedness of its occurrence. The practitioner principally concerned with infection among adults is likely to made this diagnosis too frequently. To the author's mind, cases in children which resemble the adult type should be viewed with suspicion, and are probably not tuberculous.

Tuberculosis varies with the age of the subject in its clinical manifestations in childhood. During the first two years, when resistance is low, generalized forms occur. A little later the lymphatic system forms a powerful second line of defense, and glandular tuberculosis is frequently seen. The infection may remain latent in the glands but is a continuous menace which, in the event of lowered resistance or additional infection, may result in: (1) miliary tuberculosis, often difficult to diagnose, but manifesting itself in irregular fever, cough, progressive wasting and enlargement of the spleen, and often terminating in meningitis; (2) generalized tuberculosis, which often resembles marasmus, with wasting, cough, sometimes normal or subnormal temperature until late, followed by obvious signs in the lungs, brain and abdomen; (3) tuberculosis of the bronchial glands, the commonest form of chronic tuberculous infection in childhood, with vague and indefinite symptoms and physical signs for the most part untrustworthy; (4) pulmonary phthisis, a rare form in childhood. Two other forms uncommonly met in childhood are: (1) tuberculous bronchopneumonia, usually a sequel to a simple bronchopneumonia, characterized by rapid respiration, irregular fever, emaciation and frequent pleural complications, terminating fatally; (2) epituberculosis, a rare condition in which there is consolidation usually of an upper lobe, with slight general symptoms. Recovery takes place after a period of several months.

Roentgen examination is extremely valuable in all forms of tuberculosis, but is indispensable in miliary tuberculosis and in tubercular bronchopneumonia. The interpretation of hilar shadows is often difficult. Cross-sections of blood vessels may closely resemble calcified glands. Lymphatic glands are so frequently enlarged in various infections of childhood that none should be considered tubercular unless definitely calcified. Of skin tests, the Mantoux reaction is the most reliable. The use of dilutions other than 1:1,000 is unnecessary. A positive reaction is not indicative of activity, but a negative reaction is of great significance, except in the final stages of generalized miliary infection.

SMITH, Ogden, Utah.

THE DIAGNOSIS OF PULMONARY TUBERCULOSIS IN CHILDREN. W. BURTON WOOD, Tubercle **11**:8 (Oct.) 1929.

In the past the lack of adequate means for diagnosis, reliance on untrustworthy physical signs, and perhaps the dread of missing incipient tuberculosis have led to a clouding of the issue by the too free use of such terms as "T. B. minus case,"

"potentially tuberculous child," etc. Confronted by a suspect, one has to answer a simple question: Is this child suffering from pulmonary tuberculosis? In the following conditions, a diagnosis of pulmonary tuberculosis is probably justified: (1) active pulmonary disease with positive sputum, including bronchopneumonic tuberculosis; (2) miliary tuberculosis of the lungs; (3) pleurisy with effusion, showing an excess of small lymphocytes, with or without tubercle bacilli. To these may perhaps be added cases of undoubted "juvenile infection," as shown by calcareous nodes in the lungs and calcareous deposits in the root lymph glands.

The gap between primary infection as revealed by Gohn's foci and infected hilar glands, and subclavian infiltrations typical of adolescent phthisis, has not been bridged. The juvenile type of infection is only clearly recognizable when calcification has occurred and when immediate danger has passed. It is admitted that the tracheobronchial glands are a favorite site for tuberculous infection and a potential source of miliary tuberculosis, but it is also notorious that the physical signs regarded as significant of enlarged hilar glands may be present in life, and that autopsy may prove the complete absence of such enlargement. The converse also holds true. As to the diagnostic value of paravertebral dulness, the author does not believe "that it is possible to determine the margin of an acoustic shadow in parabolic curves." Other signs appear to be equally unreliable. The roentgenogram would seem to be the only guide, and by no means an infallible one, in the diagnosis of hilar tuberculosis.

The stigma of pulmonary tuberculosis should not be placed lightly on any child. While the diagnosis remains in doubt, the child should be given the benefit of the doubt.

SMITH, Ogden, Utah.

THE DIAGNOSIS OF INTRATHORACIC TUBERCULOSIS IN CHILDREN. C. D. AGASSIZ, Tubercle **11**:14 (Oct.) 1929.

Of the manifestations of intrathoracic tuberculosis in children the most difficult to diagnose in its early stages, and the most important, is pulmonary tuberculosis. Contrary to the common teaching, the author is convinced that the manifestations of this disease in children, particularly as regards physical signs, symptoms and mode of onset, are those of the adult type; that this type is the common one and that one therefore needs to reorientate the views regarding pulmonary tuberculosis in children. Three series of cases ranging from frank pulmonary tuberculosis with positive sputum to those so slightly involved as to be almost included in so-called "incipient tuberculosis" are analyzed in support of these views.

The important points which may assist in the diagnosis of pulmonary tuberculosis in a child are: (1) a history of direct contact with a patient having tuberculosis; (2) onset with cough, hemoptysis, wasting, etc.; (3) the predominance of physical signs at the apex, and (4) roentgenologic variations from the normal. An appraisal of the series mentioned demonstrated a striking uniformity on the foregoing points, in both the mild and the severe forms of the disease.

Commenting on physical signs, Agassiz suggests that in inspecting the chest for expansion, the patient should not be too near the examiner. Differences may best be appreciated at a distance of from 8 to 10 feet (2.4 to 3 meters). Impairment of resonance on percussion over the apex may be present when one is not able to detect adventitious sounds and there is little if any alteration in breath sounds. The person in charge of the case should read the roentgenogram in conjunction with the physical signs. The points which should receive particular attention are: want of translucency at the apex; increase in striation toward one apex; marked increase in root shadows, especially if extending into a lung field and if situated at the upper level of the heart shadow; a nodular appearance near the periphery, particularly if associated with increased striation. The Pirquet reaction has a limited field of usefulness when negative, but may be of value in cases of infants and in cases of nontubercular fibrosis of the lung.

SMITH, Ogden, Utah.

CHRONIC NEPHRITIS, INFANTILISM AND CONGENITAL SYPHILIS. NOBÉCOURT and RENÉ MARTIN, Bull. Soc. de pédiat. de Paris **27**:169 (March) 1929.

A boy, aged 8 years and 7 months, showed albuminuria and edema of the lower extremities. He was well until he was 4 years of age, when he developed, for the first time, edema of the lower extremities, ascites and albuminuria. He had not had scarlet fever. He had albuminuria more or less all the time since the onset, although the edema had not recurred for two years. His diminutive height was striking; measurements during the past four years showed him to be from 9 to 17 per cent shorter than the average height for his age. He showed peg-shaped incisor teeth, which were widely separated, and carious anterior molars. He had only two carpal osseous centers, which are normally present in a child 1 year of age. There was no edema. He showed no chloride retention, but had a high blood urea. His blood p_H was 7.28, and his blood bicarbonate, 36.1, indicating a slight acidosis. His blood pressure was raised. He was pale and showed a moderate anemia. There was some left ventricular hypertrophy. The serologic test for syphilis was positive. The reported cases of renal infantilism in the English and French literature are mentioned. Although the authors realize that only an occasional case shows the presence of hereditary syphilis, they believe that in this case the presence of hereditary syphilis is responsible for both the infantilism and the chronic nephritis.

BENJAMIN, Montreal.

BILATERAL DISSEMINATED PULMONARY EMPHYSEMA DUE TO HEREDITARY SYPHILIS. E. APERT, L. GIRARD and RAPPOPORT, Bull. Soc. de pédiat. de Paris **27**:174 (March) 1929.

A boy, aged 7, developed fever, cough and dyspnea. He entered the hospital twenty-four hours later with marked difficulty in breathing and marked retraction of the chest; he was in a state of collapse and died soon after. There was no hoarseness, and no croupy quality to the cough. He had some bloody expectoration at home but none in the hospital. Both lungs were removed at necropsy. Their entire surfaces were studded with large bubbles, some of which were transparent and others yellowish-pink. The healthy lung tissue between the raised blebs occupied about the same area as the blebs themselves. On section, both lungs were studded with cavities the walls of which were glistening and seemed to be made up of pulmonary tissue. There was no fluid in these cavities. In the anterior part of the left lower lobe there was an area of consolidation with pus exuding from the bronchioles; this was the only patch which showed evidence of pneumonia throughout both lungs. Between the right upper lobe and the trachea, to the right of and behind the right innominate artery was a large indurated mass, measuring 6 by 4 by 3 cm., which on section showed hard, yellowish portions surrounded by dense fibrous bands. It resembles neoplastic rather than caseous structure within the gland. The other tracheobronchial glands are not enlarged. A few yellowish spots which were noted on the cut surface of the liver on histologic examination proved to be gummas. Microscopically, the enlarged gland in the chest showed complete replacement by sclerogummatous tissue.

The authors express their belief that the asphyxia was caused by the enlarged tracheobronchial gland pressing on the trachea, and that the very strong respiratory efforts exerted by the weakened lungs, which were infiltrated throughout by gummatous tissue, and showed obliterating arteritis, caused the unusual picture which resembled emphysema.

BENJAMIN, Montreal.

THE ROENTGEN DIAGNOSIS OF TUBERCULOSIS OF THE HILUM IN CHILDREN. GEORGE DETRE, J. de radiol. et d'électrol. **11**:257 (May) 1927.

When a roentgenologist is called on to make an examination of a child in whom tuberculosis of the lungs and the hilar glands is suspected clinically he may find a distinct picture of adenopathy with periadenitis, showing tuberculosis

of the hilum, the prognosis of which is generally favorable. These are not always the cases that are most suspicious clinically, and roentgenology renders valuable service in such cases. In other cases, he finds a picture of glands that are calcified and sometimes decreased in size in the midst of a distinct hilar arborization, showing that the process is inactive. In other cases in spite of the clinical evidence he does not find anything except a hilar shadow which is increased in density or more indistinct than normal. It is questionable whether on the basis of such observations he should make a diagnosis of sclerosis or congestion. If he does so, he runs the risk of making a diagnosis of tuberculosis of the hilum when it does not exist; on the other hand, such observations should not be ignored. Perhaps the best thing is to report them to the practitioner and let him consider them in connection with his clinical observations.

STULIK, Chicago.

A CRITICAL STUDY OF THE SYMPTOMATOLOGY OF TUBERCULOUS TRACHEOBRONCHIAL ADENOPATHY. P. F. ARMAND-DELILLE, C. LESTOCQUOY and J. VIBERT, Presse méd. **37**:1262 (Sept. 28) 1929.

The usual physical signs and symptoms attributed to tuberculous tracheobronchial adenopathy are not of much value in diagnosis, the authors believe. They show numerous photographs and roentgenograms to prove that the only reliable diagnosis is made by the roentgenogram in which a lateral view is taken instead of the usual anteroposterior view. They contend that the majority of shadows seen in an anteroposterior roentgenogram and attributed to enlarged tracheobronchial glands are, in reality blood vessels, and that true adenopathy can only be shown by a lateral view.

SANFORD, Chicago.

THE RESULTS OF "AC" VACCINATION IN INCIPIENT TUBERCULOUS AND WEAK CHILDREN. R. ARIMA, Deutsche med. Wchnschr. **55**:1208 (July 19) 1929.

Professor Arima, director of the Arima Institute for Experimental Medicine at Osaka, Japan, summarizes the reports made at various intervals by his associates on the use of tubercle bacillus protoplasm "AC" used as a vaccine. The ideal tuberculosis vaccine should accomplish two things: (1) It should protect young infants against the tubercle bacillus as cow-pox vaccination protects against smallpox. In the second place it should have a prophylactic and therapeutic value in older persons. Until the present time this has been impossible because no satisfactory vaccine has been available. With the use of "AO," however, definite advances have been made so far as the second postulate is concerned. No report can be made as yet concerning the first requirement.

The author summarizes and analyzes the eight reports in groups. These cover about 7,500 persons of all ages over a period of six years. A large majority of the patients came from the large silk spinning mills of Japan and from the schools in and around Osaka

From the results obtained in these 7,500 cases during a period of more than six years, the author draws his conclusions. The prophylactic and therapeutic vaccination of constitutionally weak persons and of those who have been exposed to the infection protects them from tuberculous processes in a manner that has not been possible heretofore. Even if the usefulness of the remedy is limited to this field it is still possible to save the second generation from exposure to tuberculosis and, theoretically, to wipe out the disease in the second generation. The question as to how long this artificial immunity will last can be answered by time alone. No doubt there must also be considerable variation in individuals. On the other hand, the immunity once acquired may possibly be maintained by the constant contact with tubercle bacilli in daily life. The method is simple and is easily carried out. Not a single unfavorable effect has been reported, and there is no danger of infection because the vaccine is not a living substance. The cost of the treatment is negligible.

SCHERER, Duluth, Minn.

A SYMPOSIUM ON CONGENITAL SYPHILIS. Verhandl. d. deutsch. path. Gesellsch. **23**:144, 1928.

G. Herzheimer-Wiesbaden declared that from 2 to 4 per cent of infants in large German cities have congenital syphilis. From 1910 to 1920 the frequency was constant; in 1922, there was an increase and during 1926 and 1927 there was a slight decrease. P. Schneider-Darmstadt discussed syphilitic osteochondritis as seen from the fifth month of fetal life to four months after birth. Periostitis was found to accompany osteochondritis constantly, at least in the region of the epiphysis. A comparison was made between the incidence of spirochetes demonstrated in them and pathologic changes in various organs.

Comparison of Incidence of Spirochetes and Lesions

	Spirochetes			Lesions		
	Stillborn, Per Cent	Dying Soon After Birth, Per Cent	Young Infants, Per Cent	Stillborn, Per Cent	Dying Soon After Birth, Per Cent	Young Infants, Per Cent
Liver	100	84	39	20	38	46
Pancreas	84	83	20	23	91	12
Lung	95	91	25	18	50	10
Spleen	96	84	33	15	38	33
Heart	83	83	29	0	8	4
Kidney	90	84	38	..	..	..

L. Pick-Berlin presented a case of late congenital syphilitic osteochondritis in a girl, aged 11 years. The long bones had undergone a marked sclerotic reaction following caseogummatous lesions, and a certain degree of sclerosis was also manifest in the ribs, phalanges and vertebrae. Wurm-Tübingen reported congenital syphilitic pulmonary lesions in a young woman. Chronic interstitial pneumonia and caseogummatous alterations were prominent but confined to the right lower lobe. The circumscribed character of the lesions led him to doubt their congenital nature. Danisch-Jena described changes in the sympathetic ganglions. The most constant of these were interstitial inflammation, retarded development of ganglion cells and the presence of spirochetes. He thinks that these changes may subsequently lead to trophic disturbances in the gastro-intestinal tract where the celiac ganglions are involved.

RUKSTINAT, Chicago.

THE HEREDITY OF TUBERCULOSIS. O. HORAK, Časop. lék. česk. **66**:411 (March 11) 1927.

The literature reveals 114 cases of hereditary tuberculosis (authentic) and 519 doubtful cases. Although syphilis and tuberculosis have much in common, the heredity of the former is conceded, while that of the latter is doubted by many authors, possibly because of the lack of positive symptoms. The author feels that there is a blood stream infection even in a great many early cases of tuberculosis. In primitive peoples no antigenic or passive protective material is found in infancy, and no protection against the virus of tuberculosis develops. Congenital immunity can be explained only on the basis of a transfer of either tubercle bacilli or immunity antibodies, with the development of congenital tuberculosis and subsequent immunity in the former instance. The present methods of immunobiologic testing of new-born infants do not reveal the presence of tubercle bacilli until after a certain ante-anaphylactic period, yet the opponents of the hereditary theory base their argument on these methods. The heredity of tuberculosis can be proved only by developing tests for ruling out the absence of tubercle bacilli, by making methodical histologic studies of fetuses of different ages, or by inoculation of experimental animals with organs of fetuses. Many authors feel that at least a part of the immunity of infants born to tuberculous parents is based on an intra-uterine infection rather than on the ordinary congenital relative immunity.

STULIK, Chicago.

Internal Diseases

PRIMARY PERITONITIS IN CHILDREN. ADOLPH G. DE SANCTIS and R. ANGUS NICHOLS, JR., Arch. Pediat. **46**:17 (Jan.) 1929.

The total number of cases of peritonitis studied was thirty-eight. They occurred in the Babies Wards of the New York Post-Graduate Hospital during the last ten years. Twenty-one, or 55 per cent, were considered primary; these are reported. The authors discuss the possible modes of infection, namely, via the blood stream, the lymph stream and the gastro-intestinal tract and, in female patients, via the external genitalia and fallopian tubes. They state that infection through the blood stream seems quite probable. Nine of the cases reported were due to *Streptococcus hemolyticus*, four to pneumococcus and one to a gram-positive bacillus; the rest were not cultured. Ten of the cases occurred in boys and eleven in girls. The ages varied from 7 weeks to 13 years, an average of 4 years. Vomiting was the initial symptom in fourteen cases. The vomitus often became stercoraceous and contained occult blood. Constipation was present in five cases and diarrhea in five. Pain apparently occurred in fifteen cases and was questionable or absent in six. The temperature ranged as high as 107 F. In 29 per cent it was 105 F. or above, and averaged from 102 to 104 F. A fluid wave was elicited in 42 per cent of the cases. The blood count was usually high, the average being 19,200; the polymorphonuclears ranged from 80 to 96 per cent. Distention was almost always present. Tenderness was present in most of the cases. Rigidity of the abdomen was absent in from 10 to 42 per cent. In ten cases the infection was attributed indirectly to acute infectious disease of the upper respiratory tract or the middle ear. In one fifth of the cases there was an underlying nephrosis. The gross mortality was 85.7 per cent. Among the eight cases in which no operation was performed the mortality was 100 per cent. Thirteen patients treated by laparotomy and drainage had a mortality of 76.9 per cent.

WILSON, Norfolk, Va.

TREATMENT OF BRONCHIAL ASTHMA. RALPH H. KUHNS, Arch. Pediat. **46**:34 (Jan.) 1929.

Asthma is a state of abnormal metabolism due to two factors, a toxemia and a lesion in the respiratory tract, most often in the ethmoid region of the nose. Bronchospasm is only a part of the clinical syndrome recognized as asthma; it is the crisis of the toxic storm and is the localized pulmonary expression of a general toxemia. Factors in the production of spasm are: an acute or chronic exposure of the nervous system to a toxic agent and an abnormally excitable peripheral sensory organ. Toxemia is the only factor common to all types of asthma. It is due to faulty metabolism and to septic absorption in varying degrees; it cannot produce bronchospasm unless ethmoid irritation is present. The patient with asthma hangs in a state of delicate balance between the absorption and the elimination of toxins. Skin sensitization tests have little value because they are too often conflicting. Treatment consists in removing all possible foci of infection, with especial attention to the ethmoid area of the nose and to the restoration of normal elimination. If the nose is involved, Dowling's method of infiltration of the nasal mucosa with colloidal silver solution is employed. Surgical intervention is used when indicated. Bronchial asthma is preventable and curable.

WILSON, Norfolk, Va.

VACCINATION AGAINST THE COMMON COLD. JOHN A. KOLMER, Arch. Pediat. **46**:41 (Jan.) 1929.

The author leans to the view that the "common cold" may be produced by one or more of the aerobic organisms and especially by staphylococci, *Micrococcus catarrhalis*, streptococci and pneumococci derived by contact with the previous

cases through "droplet" infection or that some cases may arise from organisms of this group found in the atria of the nose when sudden temperature changes, especially heat, have in some unknown manner reduced the local tissue immunity or the resistance of the nasal mucosa. In selected cases he employs a stock vaccine of the bacteria mentioned, containing 1000 million per cubic centimeter. To adults, 0.5 cc. is given as the first dose, and 1 cc at weekly intervals for three weeks. Children from 3 to 12 years of age are given from one third to one half of these amounts. If stock vaccines fail, an autogenous vaccine is prepared from a culture secured during the mucopurulent stage of an attack. This is mixed with a stock vaccine. Sixty per cent of those receiving the vaccines enjoy a freedom from common colds for a period of from four to eight months. If attacks occur earlier than four or five months after vaccination they are usually mild. There is probably a psychologic factor in the freedom from colds after vaccination in some individuals but this is not true of small children in whom the results are comparable to those obtained in adults.

WILSON, Norfolk, Va.

ESSENTIAL PENTOSURIA. JULIUS A. ROSSEN, Arch. Pediat. **46**:46 (Jan.) 1929.

Pentosuria may be divided into three groups: (1) chronic or essential, (2) alimentary and (3) complicating pentosuria.

1. Chronic or essential pentosuria: There is pentose in the urine continuously for an indefinite number of years; no symptoms of renal or pancreatic disease are present. The cause is unknown.

2. Alimentary pentosuria is transient and depends on diet. Ingestion of fresh fruits is the most common cause.

3. Complicating pentosuria may occur as a complication when dextrose is present in the urine. Pentose reduces the usual copper solutions but the reaction is slow. It does not ferment with yeast. Bial's modification of the orcein test yields a greenish precipitate and a greenish supernatant fluid with pentose. Pentose is fermented by *Bacillus coli* Escherich and *Bacillus paratyphosus* and the bacillus of Schott. It is inactive with polarized light. A case is reported. It occurs more frequently in the Jewish race. Early recognition will prevent errors in therapy and wrong to the patient and his family.

DAVIS, Norfolk, Va.

THE ANEMIAS OF INFANCY. CLIFFORD G. GRULEE, M. Clin. North America **13**:299 (Sept.) 1929.

Enough is shown of the etiology of certain varieties of the anemias of infancy to justify their classification as secondary to fairly well defined causes. The premature infant often presents an anemia of the chlorotic type which is probably due to deprivation. During its first year of life the infant depends for its supply of iron largely on that stored up during the last two months of intra-uterine life in fetal organs, especially the liver and spleen. Deprived of this source of supply on account of his premature birth, the infant's reserves are soon exhausted, and he shows a gradually increasing anemia after the second or third months. Intraperitoneal transfusion is especially helpful in this type of anemia.

Anemia due solely to nutritional disturbances is probably rare. Infections are of such frequent occurrence in infants suffering from these disorders that it is not common to find a case in which this factor may be absolutely excluded. Cases do occur, however. Simple examination of the blood may not reveal the true condition in which body fluids are much depleted. In such cases, due to reduction in blood volume the anemia may not become evident until the fluids have been restored. Simple deprivation of iron will hardly suffice to explain nutritional anemia. It is more reasonable to assume the presence of some toxic substance having a destructive action on the red cells and hemoglobin. In the pure nutritional anemias there seems to be a definite tendency for the patient to improve, and usually to react well to transfusion.

The most common variety of anemia found in infancy is that associated with infections, especially of the upper respiratory tract, and due no doubt to the action of bacterial toxins. A peculiarity of these toxins is the great variation in their specific effects on the blood in different epidemics of apparently the same infection. Until understanding of the nature and causes of respiratory epidemics is more complete, these variations must remain unexplained.

Simple varieties of anemia are often encountered in syphilitic infants. Here also the action of nonsyphilitic secondary infections have to be taken into account. Rarely, the presence of an enlarged spleen and liver and of immature cells in the blood may suggest von Jaksch's anemia.

Lead poisoning from eating paint from toys, beds, etc., occasionally causes a secondary anemia. The evidence of this perversion and the presence of stippled cells in the blood will usually identify this form. In sickle-cell anemia, the appearance of the typical cells may be delayed and may hold up the diagnosis for months. An interesting case is recounted of a paint-eating infant presenting a rather severe form of anemia, with stippled cells, in whom after several months of hospital observations, many sickle cells were finally found in the blood film.

The class of primary anemias is typified in infancy in the disease known as von Jaksch's anemia pseudo-leukemia infantum. In this condition is characteristically found immaturity of both red and white cells, with enlargement of the liver and the spleen. The prognosis in this disease appears to be more hopeful the earlier in infancy it develops. Children in whom it appears after 2 years of age seldom recover.

No form of therapy is universally successful in the anemias of infancy. When a definite cause is found and removed, much may be accomplished. Iron in the form of food appears to be as effective as when administered in other forms. Transfusion is a valuable measure in many cases, although there are many disappointments in cases of apparently the same type. Blood seems to be of the same value whether given intraperitoneally or in the vein.

SMITH, Ogden, Utah.

HYPOTHYROIDISM IN CHILDREN. E. B. REED, Nebraska M. J. **14**:441 (Nov.) 1929.

Types of hypothyroidism are designated as mild, moderate and severe. Mental defects are more serious than physical. Roentgen examination is of value in diagnosis; the basal metabolism in young children is difficult to obtain. Iodized cod liver oil is recommended for treatment.

HAMILTON, Omaha.

THE LEUCOCYTE COUNT IN RHEUMATIC HEART DISEASE IN CHILDHOOD. C. BRUCE PERRY, Arch. Dis. Childhood **4**:247 (Oct.) 1929.

In forty-one children who were seen in various stages of rheumatic heart disease, 239 leukocyte and differential counts were made. Acute carditis was associated with mild leukocytosis and an increase in neutrophils. The count, however, was of no value as an index of activity.

PETERMAN, Milwaukee.

STUDIES OF PNEUMONIA IN CHILDHOOD: V. EMPYEMA. CHARLES MCNEIL, AGNES R. MACGREGOR and W. ALISTER ALEXANDER, Arch. Dis. Childhood **4**:270 (Oct.) 1929.

In a series of 648 cases of pneumonia in children up to 12 years of age, empyema occurred in 89. The total mortality was 40.5 per cent. There were 53 boys and 36 girls. The antecedent pneumonia was lobar in 45 cases, with six deaths; bronchial in 13 cases, with 13 deaths, and undetermined in 31 cases, with 17 deaths. Complications were: pericarditis, 16; peritonitis, 7, and meningitis 2.

PETERMAN, Milwaukee.

NOTE ON THE BACTERIOLOGY OF BRONCHO-PNEUMONIA OF CHILDREN. W. GLEN LISTON, Arch. Dis. Childhood **4**:283 (Oct.) 1929.

Bacillus influenzae was found in 95 per cent of the forty cases of broncho-pneumonia studied with McNeil, Macgregor and Alexander in their previously reported studies. In the early and acute cases lung puncture gave an almost pure growth. It is Liston's opinion that Pfeiffer's bacillus is the primary agent in bronchopneumonias, and that this organism opens the way for invasion by a secondary organism.

PETERMAN, Milwaukee.

THE ACID-BASE EQUILIBRIUM OF THE BLOOD IN ACUTE RHEUMATISM. LEONARD G. PARSONS and S. H. EDGAR, Arch. Dis. Childhood **4**:291 (Oct.) 1929.

The acid-base equilibrium in fifty-three children in various stages of rheumatic diseases was studied and compared with the equilibrium of fifteen normal persons. The p_H was determined electrometrically. The acid-base equilibrium in children with rheumatism was found to be entirely normal.

PETERMAN, Milwaukee.

THE CARDIAC CLINIC AND HOSPITAL: THEIR VALUE IN THE CONTROL OF THE RHEUMATIC INFECTION. LEONARD FINDLAY, JAMES W. MACFARLANE and MARY M. STEVENSON, Arch. Dis. Childhood **4**:306 (Oct.) 1929.

Since 1923 the authors have conducted a cardiac clinic. It is their conclusion that the regular supervision of patients at a cardiac or rheumatism out-patient clinic did not diminish the recurrences of the rheumatic infection or affect the progress of rheumatic heart diseases. Residence in the country under medical supervision seemed to control the rheumatic infection. It is suggested that the chief attention be directed to prophylaxis by a modification of environment.

PETERMAN, Milwaukee.

NONTUBERCULOUS PLASTIC PLEURISY IN CHILDREN. WALTER M. WHITAKER, Arch. Dis. Childhood **4**:323 (Oct.) 1929.

Two cases of spontaneous dry pleurisy are presented. The tuberculin tests were negative.

PETERMAN, Milwaukee.

PULMONARY EMBOLISM IN CHILDHOOD. J. M. SMELLIE, Arch. Dis. Childhood **4**:328 (Oct.) 1929.

A case of pulmonary embolism in a child, aged 9, is presented, together with the results of postmortem examination. The thrombus extended from the right auricle through the tricuspid valve and through the right ventricle and pulmonary valve into the pulmonary artery.

PETERMAN, Milwaukee.

CONGENITAL CARDIAC DISEASE IN IDENTICAL TWINS. K. SHIRLEY SMITH, Arch. Dis. Childhood **4**:330 (Oct.) 1929.

Congenital cardiac defects in twins are discussed. A case of patency of the ductus arteriosus is described as a solitary cardiac defect in both of a pair of twins. The twins were probably identical.

PETERMAN, Milwaukee.

CHANGES IN THE BLOOD CHEMISTRY IN CONGENITAL HYPERTROPHIC PYLORIC STENOSIS AND THEIR CLINICAL SIGNIFICANCE. STANLEY GRAHAM and NOAH MORRIS, Arch. Dis. Childhood **4**:335 (Oct.) 1929.

The most striking clinical manifestation of alkalosis in these cases is the depressed breathing. The rate and amplitude are markedly diminished and there

are periods of apnea associated with a general lethargy. There is a striking relationship between the carbon dioxide content of the blood and the respiratory rate. There is some relationship between the depletion of the blood chloride and the severity of the vomiting. The alkalosis is probably produced by the loss of chlorine from the body. The total carbon dioxide varies inversely with the blood chlorides. The fixed base is usually unaltered.

PETERMAN, Milwaukee.

TWO CASES OF CHRONIC HYPERPLASIA OF THE RIGHT SIDE OF THE UPPER JAW. H. BELL TAWSE, Proc. Roy. Soc. Med. **22**:1525 (Oct.) 1929.

The first case reported was that of a girl, aged 15, who complained of swelling of the right side of the upper jaw for twelve months. A roentgenogram showed uniform density of the body of the superior maxilla. An exploratory operation was performed through the canine fossa, and normal cancellous bone was scooped out with a curet. The pathologic report showed a dense network of bony trabeculae, with many osteoblasts and a few osteoclasts. No sign of an inflammatory reaction or of malignant disease was found. The second case reported was in a boy, aged 9. Swelling which followed a blow on the right upper jaw had been present for twelve months. Roentgenograms showed increased density of the right superior maxilla and the zygoma, which was due to osteitis. There were no signs of malignancy. An exploratory operation through the canine fossa revealed the same conditions as in the previous case.

WILLIAMSON, New Orleans.

SPLENIC ANAEMIA WITH HAEMATEMESIS. J. WILKIE SCOTT, Proc. Roy. Soc. Med. **22**:1526 (Oct.) 1929.

This case was reported in a girl, aged 12 years, who was apparently healthy until March 9, 1929, when she suffered an attack of hematemesis. Two days later, she was admitted to the hospital with severe hematemesis and in profound collapse. The liver was slightly enlarged. The spleen was also enlarged. On March 17, ascites commenced and steadily increased. On April 19, paracentesis was performed. The child was still very ill. Transfusion was performed. By April 24, the general condition had improved. Blood counts showed leukopenia and diminished platelets. Since the case was reported, the spleen weighing 23 ounces (652 Gm.) was removed and patient was discharged as recovered.

WILLIAMSON, New Orleans.

TWO CASES OF GROWTH ON CLAVICLE. F. CROOKS, Proc. Roy. Soc. Med. **22**:1529 (Oct.) 1929.

A patient, aged 13 years, noticed a swelling at the inner end of the left clavicle about three months before admission to the hospital. The swelling was the size of a duck's egg, hard, smooth, fixed and tender. A roentgenogram suggested chronic osteomyelitis. At operation, the inner half of the clavicle and the articular surface of the sternum were excised. The report from the pathologic laboratory gave fibroma.

The second case reported was in a girl aged 4½ years. She gave a history of injury. The swelling was also the size of a duck's egg and involved the inner third of the right clavicle. The same operation was performed. The pathologic report gave sarcoma.

WILLIAMSON, New Orleans.

OSTEO-ARTICULAR DWARFISM IN ARTHRITIS DEFORMANS. G. MARINESCO and J. F. CLAUDIAN, Arch. de méd. d. enf. **32**:633 (Nov.) 1929.

Clinical knowledge of arthritis deformans is of comparatively recent date and its pathogenesis is still obscure. Claudian, in a previous thesis, collected only 150 cases. Two further cases are reported in this contribution: Young girls who were stricken at the age of 7 and were followed to their twentieth year.

The evolution of the disease being practically identical during these years, the cases are discussed as one. Following the usual brusque onset commonly noted in these patients, the large articulations were attacked, one after the other. The joints were swollen, the surrounding integument became inflamed and there was extreme pain. In a short time the jaw, the joints of the fingers and finally the spinal articulations were involved. At this point, the fever disappeared and the pain became more endurable, but excessive perspiration and swelling persisted. In two years from the initial attack, akinesia was complete; there remained only limited movement in the coxofemoral and a few of the finger joints. Various forms of treatment, efficient in other varieties of rheumatism, such as the administration of salicylates, sun baths, mud baths, etc., were attempted but resulted in no amelioration of the condition. Roentgenograms revealed true ankylosis with general osseous decalcification in which the bones of the cranium shared. Another striking feature in these cases was the astonishing atrophy of the lower jaw following partial immobilization of the temporo-maxillary joint. This phenomenon was found in only four instances among the 150 observations reported in the literature. Growth having been arrested intermittently, there was pronounced disproportion between the different segments of the body; the cranial circumference, for example, while less than normal for age, was much greater than that for a child of the corresponding height. Secondary sexual characteristics were well marked but one patient suffered from amenorrhea. In spite of these observations, the authors feel inclined to classify these as cases of dwarfism, with etiology obscure, in contrast to those of hereditary origin, of myxedematous, achondroplastic, osseous and toxic sources. They also distinguish it from infantilism, cerebration being normal for age, and from dystrophies of endocrine origin on account of the total absence of symptoms denoting thyroid, hypophyseal or ovarian deficiency. The conclusion is made that the process is entirely an infectious one, involving coincidently the vegetative nervous apparatus, as shown by the hyperidrosis, excitability and vasomotor disturbances, and the articular surfaces of the joints—a trophoneurotic syndrome, general and local, leading to complete and permanent arrest of function.

AMESE, Denver.

SEVERE ANEMIA RELIEVED BY THE FEEDING OF CALF'S LIVER AND TRANSFUSION: DIAPHRAGMATIC HERNIA OF THE STOMACH. NOBÉCOURT and G. BOULANGER-PILET, Bull. Soc. de pédiat. de Paris **27**:190 (March) 1929.

A boy, aged 32 months, was admitted to the hospital. He was extremely pale, of a yellowish-white, waxy color, and had edema of the eyelids and cold extremities. His pulse was small and rapid and there was an apical systolic murmur which could also be heard over the great vessels of the neck. There was no adenopathy. The liver was of normal size. The spleen was palpable 4 cm. below the costal margin. There was no evidence of hemorrhage. Tests for tuberculosis and syphilis were negative. The blood showed: red blood cells 1,810,000; white blood cells, 5,500; hemoglobin, 30; slight poikilocytosis and anisocytosis and 1 per cent nucleated red cells. Bleeding time was five minutes, and coagulation time, fifteen minutes. The gastric juice showed a low acidity. The feces showed some undigested muscle fibers, a large amount of neutral fats, and no parasites or parasitic ova. Roentgenologic examination showed a prolongation of the stomach into the right side of the thorax above the diaphragm. This may have accounted for the frequent vomiting of the child since birth, the vomiting ceased with the improved general condition, so that no surgical intervention was advised. The child was always malnourished and had marked anorexia. The authors do not know what the cause of the anemia was, but they believe that the daily ingestion of 50 Gm. of boiled calf's liver, followed by numerous subcutaneous injections of 30 cc. of the father's blood, was responsible for the child's marked improvement. Later the child was given liver extract for a month and the red cell count was further increased. The child gained weight consistently and was cured.

BENJAMIN, Montreal.

NONTUBERCULOUS PNEUMOTHORAX IN INFANTS. P. LEREBOULLET, M. LELONG and R. EVEN, Nourrisson **17**:257 (Sept.) 1929.

Two new cases of nontuberculous pneumothorax in infants are reported and forty-three others are reviewed from the literature; this signifies that these cases occur more frequently than is generally supposed. In infants the nontuberculous variety of pneumothorax is more common than the tuberculous, and is usually dependent on an acute pulmonary infection: pneumonia, bronchopneumonia, pulmonary abscess or whooping cough.

The mechanism is either the direct rupture of an abscess into the pleural cavity or the bursting of a localized patch of emphysema.

The authors describe two varieties and illustrated them by their own case reports: (1) the acute form which is in all respects similar to the acute pneumothorax occurring in adults, and (2) a latent form peculiar to infants and discovered accidentally either by physical signs, by roentgen examination or at autopsy.

The most valuable aid in diagnosis is fluoroscopy.

The treatment and prognosis depend on the cause. If the pneumothorax is accompanied by a suppurating empyema, the outlook is poor; if the pleural cavity remains dry, recovery is the rule.

McCLELLAND, Cleveland.

THE HEMORRHAGIC SYNDROME IN THE CHILD: I. CLINICAL TYPES. E. MEDDA, Riv. di clin. pediat. **27**:655 (Sept.) 1929.

Among 7,090 sick children coming to the Pediatric Clinic at Bologna between 1903 and 1927, there were 35 cases of purpura hemorrhagica, 11 cases of Schoenlein's and Henoch's purpura, 7 cases of hemophilia, 11 cases of scurvy and 17 cases of a secondary hemorrhagic diathesis; the total number of cases showing hemorrhagic manifestations was 81 (1.14 per cent). Of these 81 patients, 9 died—6 because of intercurrent or concomitant infections, and 3 (3.7 per cent) because of the hemorrhagic condition itself.

Five cases, one of each of the aforementioned types, are discussed, the observations on the blood and the results of the measurement of capillary resistance being given.

HIGGINS, Boston.

THE HEMORRHAGIC SYNDROME IN THE CHILD: II. ETIOLOGY, PATHOGENESIS. E. MEDDA, Riv. di clin. pediat. **27**:674 (Sept.) 1929.

In this paper, the author discusses the etiologic factors in hemorrhagic syndromes, citing many references on this subject. These factors fall into three groups: constitutional, toxic, and infectious. He quotes from the data obtained from eighty-one patients (thirty female and fifty-one male) observed in the clinic at Bologna.

A history of hereditary hemorrhagic manifestation, either similar or dissimilar to that shown by the patient, was obtained in 25 of the 81 cases; in 11 of 35 with Werlhof's purpura, in 3 of 11 with Schoenlein-Henoch's purpura, in 6 of 7 with hemophilia, in 1 of 11 with scurvy and in 4 of 17 with secondary hemorrhagic syndrome.

The main toxic causes of purpura are medicines (neoarsphenamine, antipyrine, phosphorus, phenolphthalein, etc.) and gastro-intestinal disturbance. Of the 81 cases, 13 per cent showed vomiting, 21 per cent blood in the feces, 30 per cent indicanuria, 9 per cent acetonuria and 29 per cent irregularity of the bowels; these observations were unusually frequent in Schoenlein-Henoch's purpura.

Fever was found in 41 per cent of the cases: in 28 per cent of the cases of Werlhof's purpura, in 72 per cent of those of Schoenlein-Henoch's purpura, in 76 per cent of those of secondary hemorrhagic syndrome, in 27 per cent of those of scurvy and was not found in any case of hemophilia; 24 per cent of the cases gave a positive reaction to the skin tuberculin test, and 6 per cent a positive reaction to the Wassermann test.

HIGGINS, Boston.

PERIODIC INFANTILE ACIDOSIS. EUGENIO CIENFUEGOS, Arch. latino-am. de pediat. **23**:577 (Aug.) 1929.

The causative factor in a majority of the cases of infantile acidosis is an infection.

The focus of this infection is generally in the digestive tube or in neighboring structures which drain their infected material into the tract.

It does not appear that anaerobes play an important rôle in the development of such infections.

Constitutional conditions, such as exudative diathesis or neuropathic or lymphatic diathesis of hereditary syphilis, play a secondary rôle. The treatment must aim to combat the infection. The auto-enterovaccine therapy combined with an adequate alimentary regimen will give the best results. Collateral foci should be removed if possible.

SCHLUTZ, Minneapolis.

PRIMARY SARCOMA IN THE LUNG OF A CHILD OF EIGHT YEARS. M. ACUNA, PERLINA WINOCUR and GERMAN P. OROSCO, Arch. latino-am. de pediat. **23**:605 (Aug.) 1929.

The symptoms in the case developed five months before admission to the hospital and began with persistent cough and occasional pain in the left inframammary region. The temperature was continually elevated to 38 and 39 C. (100.4 and 102.2 F.).

The roentgenogram showed displacement of the heart shadow to the right and a dense shadow over the lower base of the left lung.

Death ensued four weeks after admission, following the development of intense dyspnea and cyanosis.

At autopsy a sarcoma of the left lower lobe of the lung was found as a primary lesion. There was a slight metastasis in the liver.

The authors give an excellent statistical review of various primary malignant tumors, and the organs most commonly affected in the child.

SCHLUTZ, Minneapolis.

LIPOID NEPHROSIS IN A CHILD AGED TWO YEARS. MARIA LUISA SALDUM, Arch. latino-am. de pediat. **23**:619 (Aug.) 1929.

The symptoms in the case began insidiously with asthenia and lumbar pains with subsequent development of local and generalized edema. Renal elimination was normal. There was excessive albuminuria. The blood showed hypoalbuminemia and marked increase of cholestrin.

No etiologic factor could be determined in the case. An aggravated and prolonged pyodermia during the first year of the infant's life may have been a causative factor.

The author inclines to the theory of Munck and others who believe that the disorder is primarily caused by metabolic dysfunction in the protein metabolism and in the lipoids, notably cholesterin.

SCHLUTZ, Minneapolis.

ERYTHROBLASTIC MYELOSIS IN INFANCY. JUAN ORRICO, Arch. latino-am. de pediat. **23**:679 (Sept.) 1929.

The author reports two cases: those of a child, aged 4, and of another aged 3 years, showing an erythroblastic myelosis.

The first case showed a pseudoplastic anemia and erythroblastic myelosis. It resembled the aleukemic type described by Ghedini.

The red cells varied in number between 970,000 and 500,000 per cubic centimeter; the white cells, between 9,000 and 3,000, and the hemoglobin between 18 and 9 per cent (Sahli).

The second case resembled the pernicious anemia type described by Di Guglielmo (La Eritemie, *Hematologica,* 1928, p. 301).

In the blood picture there was a diminution of the red cells (2,000,000)—a discrete leukocytosis. The hemoglobin index was 1. There was slight lymphocytosis (45 per cent). Normoblasts to the extent of 27,000 per cubic centimeter of blood were found.

The red cells showed embryonic characteristics. There were many macrocytes and microcytes, some showing active karyokinesis.

There was complete absence of megaloblasts. There was no enlargement of the spleen or the liver. The Wassermann, von Pirquet and Mantoux tests were negative. Slight elevation of temperature was constantly present.

SCHLUTZ, Minneapolis.

THE SYNDROME OF BANTI. D. PEDRO CALAFELL, Med. de los niños **30**:244 (Aug.) 1929.

In the early stage it is difficult if not impossible to differentiate Banti's disease from other forms of splenomegaly with anemia. In the second stage the diagnosis is made easier by the enlargement of the liver, the increased density and reddish color of the urine, and the presence of traces of urobilin. The erythrocytes are usually between 2,000,000 and 3,000,000; the leukocytes from 4,000 to 5,000, and the hemoglobin from 25 to 30 (Sahli). In the late stage, Banti's disease may be confounded with the cirrhosis of Laennec. However, the splenomegaly is more marked and the alteration in the blood more characteristic in Banti's disease.

Splenectomy performed early results in a cure in 50 per cent of the cases. Specific infections, such as hereditary syphilis and malaria, should be looked for before advising splenectomy.

DWYER, Kansas City, Mo.

SPONTANEOUS BILATERAL PNEUMOTHORAX IN A CASE OF POLYCYSTIC LUNG. A. SCHMINCKE, Beitr. z. path. Anat. u. z. allg. Pathol. **80**:692, 1928.

A woman, aged 24, developed bilateral pleural effusion about a year before her admission to the hospital. The fluid was clear and contained no cells or tubercle bacilli. The difficulty in respiration with which she suffered was relieved by withdrawal of the fluid, but returned and was her chief complaint on admisison. At this time she was found to have bilateral pneumohydrothorax. No evidence of tuberculosis could be found. The respiratory difficulty was again relieved by withdrawal of the fluid, but recurred from time to time as the fluid reaccumulated. She died after continuation of such symptoms for three fourths of a year. At necropsy, the lungs were compressed and each pleural cavity contained air and free, clear fluid. There were no adhesions and no tuberculous lesions. Beneath the pleura of each lung were numerous air-filled blebs, some of which had perforated through the covering pleura, thus giving rise to the pneumothorax. The dilated air spaces were limited to the peripheral portions of the lungs and were in communication with the bronchial system. They were the dilated portions of the incompletely developed terminal bronchi. Accepting Bender's description of the development of the lung, Schmincke concludes that terminal embryonic bronchi in the peripheral portions of the lung, which are the last portions to complete their embryonic development, did not go on to the formation of air alveoli. The process is considered one of inhibition or Hemmung of fetal development, and Schmincke calls attention to the similarity of the condition described by him, considered the first reported case of its kind, to fetal bronchiectasis and congenital cystic lung, for which embryonic maldevelopment of the kind described offers the best explanation. Cystic dilatation of the undeveloped bronchi, in the walls of which there is little elastic tissue, follows. A case of spontaneous bilateral pneumothorax, identical with that reported by Schmincke, has been briefly described in Abt's "Pediatrics," vol. 4, chapter 65, p. 33.

[ARCH. PATH.]

THE DEVELOPMENT OF HEART-BURN: A CLINICAL AND EXPERIMENTAL STUDY. O. PORGES and D. O. STERNBERG, Wien. Arch. f. inn. Med. **18**:379, 1929.

The authors believe that the following factors contribute to the development of heart-burn.

1. The influence of irritant fluids on the mucous membrane of the lower part of the esophagus. The acid secretion of the stomach or, in exceptional cases, the alkaline secretion of the intestine, may cause this irritation.

2. Abnormal motility of the stomach causing the gastric contents to enter the lower esophagus. Gastritis or pyloric stenosis may cause such abnormal motility.

3. An esophagitis may be produced by the continued irritation of the gastric secretion or by other causes.

SCHLUTZ, Minneapolis.

THE USEFULNESS OF PEPTIDASE DETERMINATIONS IN THE DIAGNOSIS OF LIVER DISEASE. L. BÖHMIG, Wien. Arch. f. inn. Med. **19**:89, 1929.

The presence of peptidase and its volume are fairly constant factors in the normal organism. In the presence of abnormal conditions, particularly disease of the liver, these factors change. These changes can be used as a measurable index of disease of the liver.

In acute disease of the liver the level of peptidase is increased in the serum and remains normal or only slightly increased in the urine. In chronic disease of the liver the situation is reversed. The peptidase content of the blood serum remains normal while that of the urine is increased.

Urobilinuria and increase of peptidase excretion both occur if there is functional damage of the liver along with destruction of the parenchyma.

SCHLUTZ, Minneapolis.

COMPARATIVE LIVER FUNCTION TESTS. VIKTOR WEISS and L. HOLLÓS, Wien. Arch. f. inn. Med. **19**:101, 1929.

The authors consider the following liver function tests of value: (1) qualitative and quantitative determination of bilirubin in the blood, (2) determination of the bilirubin content of the duodenal content, (3) the indigo carmine test, (4) determination of urobilinuria and (5) determination of alimentary galactosuria.

All of the tests mentioned can be carried on within a period of forty-eight hours.

The information obtained by these comparatively simple methods is fully as valuable as that obtained by more complicated and time-consuming methods.

SCHLUTZ, Minneapolis.

TREATMENT FOR ABSCESS OF THE LUNGS. BLANKA BOHMOVA, Časop. lék. česk. **66**:373 (March 4) 1927.

Arsphenamine is recommended in the treatment of pulmonary abscess and gangrene, especially in those cases showing *Spirillum*. Staehelin collected a series of fifty cases in which arsphenamine was used, with 60 per cent healing and 40 per cent improvement. In various series the postoperative death rate was from 40 to 70 per cent. Dorendorf claims that many cases heal spontaneously under heliotherapy, Quinke posture, Williams dry diet and fresh air. The report of a case is given.

STULIK, Chicago.

INSULIN-GLUCOSE TREATMENT OF CYCLIC VOMITING. KENKICHI ITO, J. Pediat. (Tokyo), no. 352, Sept. 20, 1929, p. 1496.

The author treated five patients with severe cyclic vomiting in childhood. All the cases showed at one time or another various degrees of acetonuria, as determined

by the Lax method. The amount of acetone present, as determined by this method, varied from 0.0091865 Gm. per five-tenths cubic centimeter of urine to 0.00410975 Gm.; all of these amounts were reduced to none in from 94 to 230 hours after the rectal administration of from 300 to 350 cc. of a 5 per cent solution of dextrose, followed shortly afterward by a subcutaneous injection of from 2 to 4 units of insulin (Toronto).

KATO, Los Angeles.

Nervous Diseases

ENCEPHALITIS PERIAXIALIS DIFFUSA. WALTER D. SCHELDEN, JOHN B. DOYLE and JAMES W. KERNOHAN, Arch. Neurol. & Psychiat. **21**:1270, 1929.

A clinical and pathologic report of two cases of so-called Schilder's disease is made by Schelden and his co-workers.

In both cases the macroscopic changes were characteristic of Schilder's disease: large areas of degeneration of the subcortex, and absence of involvement of the gray matter of the cortex or only of its deeper layers. The degeneration in this disease usually starts in the occipital, but may also start in the frontal lobe.

Microscopic changes were: early breaking up of the myelin, followed by that of the axons which generally suffer less severely; both the myelin and axons break up into smaller fragments and become finally transformed into lipoids which are taken up by scavenger cells (gitter cells). The glia shows marked progressive changes, especially in the form of proliferation of astrocytes and the appearance of large numbers of giant cytoplasmic cells ("gemästet") glia cells. It is remarkable that the type of glia cells known as oligodendroglia showed in these cases regressive changes in the form of so-called swollen oligodendroglia. A wall of hyperlastic astrocytes was seen between the degenerated and the normal tissues. Microglia was abundant and satellitosis was present in the advanced stages. So-called mucocytes, that is, cells containing mucus, were absent but were present within the perivascular spaces. These contained masses of scavenger cells mixed with lymphocytes, few polymorphonuclear cells but no plasma cells. It is evident that in contrast to the gross pathologic changes, the microscopic picture of Schilder's disease shows nothing specific, nor is the clinical picture characteristic. However, in the first patient, a boy aged 7 years, the diagnosis has been made before the patient's death, from the following symptoms: apathy, change of personality, rapid onset of blindness and deafness, bulbar symptoms with signs of involvement of the motor and sensory neurons and frequent convulsions. The course was rapid. The patient died four months after the onset. Previous diseases were various infectious diseases of childhood and preceding the onset there was a bilateral otitis media.

In the second case, the patient was a woman, aged 27. Six and one-half weeks prior to admission to the hospital she had been delivered of her first child by forceps; two and a half weeks later visual disturbances set in—blurring of vision followed by complete blindness within one week; later, facial weakness developed with weakness and partial paralysis of the left side of the body; generalized tremor, involuntary evacuations and coma. Death followed two months after onset. Here the actual condition was not recognized and an abscess of the brain was considered probable. A craniotomy was done but no abscess was found.

HASSIN, Chicago.

PNEUMOCOCCUS MENINGITIS: REPORT OF CASE IN NEW-BORN INFANT, WITH RECOVERY. J. S. UHR, Arch. Pediat. **46**:121 (Feb.) 1929.

The literature dealing with recoveries is reviewed and a recovery reported. Symptoms were noted the sixth day of life; lumbar puncture was done the third, seventh and ninth days of illness. Coincident with the meningitis there was an acute nephritis. The pharynx appeared to be the portal of entry. No therapeutic measure except lumbar puncture is suggested.

WILSON, Norfolk, Va.

AMAUROTIC FAMILY IDIOCY WITHOUT THE CLASSICAL CHERRY-RED SPOT. J. EPSTEIN, Arch. Pediat. **46**:124 (Feb.) 1929.

A case of amaurotic family idiocy is reported in an infant, aged 7 months, a child of a young Russian Jewess. She was the fourth child; the first child, a boy, died of this disease.

Repeated ophthalmoscopic examinations did not reveal a cherry-red spot. The course of the disease was that of amaurotic family idiocy, but without the cherry-red spot, hence of the Tay-Sachs' type. Death occurred at the age of 20 months and 1 week.

WILSON, Norfolk, Va.

MONGOLISM IN ONE TWIN. R. H. SHATTUCK, J. A. M. A. **92**:1593 (May 11) 1929.

The author reports a case of mongolism occurring in one of twins.

BONAR, Salt Lake City.

PERSONALITY CHANGES IN CHILDREN FOLLOWING CEREBRAL TRAUMA. J. KASANIN, J. Nerv. & Ment. Dis. **69**:385 (April) 1929.

The author finds that in 10 per cent of cases of the Judge Baker Foundation in which the conditions were diagnosed as psychopathic personalities the patients had had serious injury to the brain during childhood or adolescence, with either fracture of the skull or severe concussion of the brain. A control group of 120 cases not showing psychopathic tendencies showed only 2 cases of serious injury of the brain. Following Trotter, he regards the three important characteristics of concussion as: instantaneous onset, loss of consciousness and circulatory failure. Trotter found headaches, giddiness, tinnitus, memory defects and slight changes in disposition as signs of incomplete recovery from such concussion. Cannon's discovery that a brain deprived of its blood supply will take up water from a solution isotonic with the blood, thus causing further swelling, may be applied to swelling which occurs after severe cerebral concussion observed at autopsy.

Pierce Bailey, in 1903, reported irritable, boisterous, uncontrollable behavior in children after cerebral injury. Adolf Meyer, in the same year, showed instances of fatigue, retardation of thought, impaired memory, irritability, headaches and extreme susceptibility to alcohol in adults from the same cause.

The author presents, in some detail, fifteen cases of children with personality changes following trauma. Thirteen of these were regarded as psychopathic, having first been treated as functional cases with prolonged and unavailing psychotherapy and social study. He is of the opinion that severe injury of the brain interferes with the formation of the proper inhibitory influences in the integration of the child's personality. Encephalography by the lumbar route should be used more extensively in the study of these cases. When psychotherapy fails, persons should receive prolonged and intensive training in correctional institutions under intelligent supervision. The outlook is more favorable than in the behavior disorders subsequent to encephalitis.

HART, New York.

DIAGNOSIS AND TREATMENT OF POST-ENCEPHALITIC PARKINSONISM. FREDERICK L. PATRY, J. Nerv. & Ment. Dis. **69**:617 (June) 1929.

Epidemic encephalitis is regarded as in infectious disease, the toxic products of which have a special affinity for the gray matter of the central nervous system, causing widely spread lesions. The parkinsonian syndrome is found chiefly in adults. It behaves like a chronic disease. Its onset may be acute or insidious. There are a multitude of different symptoms, due to the widespread nature of the lesions. The disease may be dormant for from weeks to years, becoming active again in the striking parkinsonian picture. Reduction of strength, weariness, insomnia, greasy face, fixed expression, staring eyes, sialorrhea, muscle tremor

and rigidity, with muscle palsies, myoclonus and pupillary abnormalities are the most characteristic symptoms. Early symptoms, such as neuritis, neuralgia, cutaneous hyperesthesia and irregular pyrexia or mental symptoms, may precede the development of the parkinsonian state. In children the effects are chiefly in the psychic sphere; the intensity and type or duration of the acute phase seem to have no correlation with the severity or character of the mental or physical sequelae. No special treatment is known, but hyoscine hydrobromide, given in increasing doses from $\frac{1}{200}$ to $\frac{1}{50}$ Gm. three times a day, both by mouth and subcutaneously, gives the greatest relief. Ultraviolet light, physical exercise and occupational therapy are also valuable. Foci of infection should be sought and removed. The improvement from hyoscine continues only as long as the drug is given, but no untoward symptoms are noted, even over a period of years.

HART, New York.

THE TREATMENT OF ACUTE EPIDEMIC ENCEPHALITIS. FRANCIS W. HEAGEY, Minnesota Med. **12**:121 (March) 1929.

In the treatment for acute epidemic encephalitis (1) diagnosis is the most important requisite; then come (2) absolute rest in bed and freedom from stimuli; (3) repeated lumbar punctures; (4) removal of foci of infection at a suitable time, and (5) psychotherapy and physiotherapy directed toward the restoration of the patient's confidence both in his mental and in his physical functions.

HUENEKENS, Minneapolis.

MENTAL INEFFICIENCY IN SCHOOL CHILDREN. THOMAS FERGUSON, Edinburgh M. J. **36**:526 (Sept.) 1929.

The author reports an investigation of the children in two fields: from a mixed population and from an industrial county borough. The survey deals with a school census of the children who are mentally deficient, a consideration of the special schools for mentally feeble children, and the maintenance of classes for the backward in ordinary schools. Head teachers were asked to select those children whom they regarded as subnormal or unstable. From a school population of about 12,000, 308 were referred for examination. Only 12 of these selected by the teachers were found to be of normal intelligence; 140 were dull or backward, 131 were feeble-minded and 25 were imbecilic. In all these groups, 30 children were regarded as mentally unstable. The author expresses his feeling that such cases offer to the psychologist a great opportunity for work. Some of these children are dangerous in their influence on ordinary or subnormal children.

These figures give about 11 defective children to each 1,000 children on the school register; one will gain no idea of the general prevalence of feeblemindedness from these figures obtained in the schools, for many of school age are not eligible for enrolment. The groups containing the older children will show up the defectives glaringly. The effort should be made to find these "difficult" children early in school life.

The examination for determining the children's abilities showed that they were lowest in arithmetic, slightly higher in handiwork, while they did somewhat better in writing and reading. Physical defects that aggravated the mental condition were found in 70 children; among these there were 18 children with tuberculosis, 15 with defective vision and 8 with deafness.

Special schools are of value if not made the dumping ground for low grade defectives, though there is a tendency to expect unreasonable results from such schools. Pupils and teachers must be carefully selected. Children with an intelligence quotient from 0.50 to 0.65 show the most good from special schooling, but an experienced physician for this line of work will be of even greater value in overhauling these children. Their progress in backward classes is discussed at length by Ferguson. This article should be read by all who are interested in special schools.

NEFF, Kansas City.

THE ARNETH BLOOD-COUNT IN IDIOCY AND LOW-GRADE IMBECILITY, WITH SPECIAL REFERENCE TO THE INCIDENCE OF TUBERCULOSIS AND TUBERCULAR INFECTIONS. STANLEY R. TATTERSALL and CYRIL J. THOMAS, J. Ment. Sc. **75**:64 (Jan.) 1929.

The number of nuclear lobes in 100 polymorphonuclear leukocytes of the blood (the Arneth count) is very low in idiots and imbeciles as compared with that in normal persons and low as compared with that in psychotic patients. Of 142 feebleminded persons studied, the averages for males were: imbeciles 192 and idiots, 177; for females: 195 and 181, respectively. The figures therefore appear to be lower for the more defective types and slightly higher for females than for males. The authors, who regard this count as in some way an "index of vitality," consider the reversal of the usual higher index in males than females as the result of the observed better physique in the females of this series. The principal value of a low count, however, is an index of some infective process, especially of tuberculosis. Clinical arrest of a tuberculous process is in all cases accompanied or preceded by a rise in the count.

SINGER, Chicago.

INFANTILE DEMENTIA. H. JANCKE, Arch. f. Kinderh. **88**:114 (Aug. 20) 1929.

Jancke reports two cases of infantile dementia, one in a girl, aged 2 years, and one in a girl, aged 3 years and 5 months. In the first case the condition appeared when the patient was only 1 year and 8 months of age. This is the earliest appearance of infantile dementia thus far reported. There have been thirteen cases reported in the literature, almost all of them occurring in Austria and Russia. The author believes that infantile dementia is caused by a diffuse organic injury of the brain which leads to a general lowering of the mental processes but is without marked influence on the bodily processes.

SANFORD, Chicago.

A CASE OF IDIOTIA THYMICA. J. S. GALANT, Arch. f. Kinderh. **88**:275 (Oct. 25) 1929.

The author's case occurred in boy aged 17 years with the physical development of 8 years. The circumference of the head was 51 cm., and the bones of the leg were 64 cm. long. The differential diagnosis lay between eunuchism, which shows no loss of mental power, and hypothyroidism, which has basal metabolic changes.

SANFORD, Chicago.

THE DIAGNOSIS AND PROGNOSIS OF EPILEPSY IN CHILDHOOD. GERTRUD REMÉ, Monatschr. f. Kinderh. **45**:228 (Nov.) 1929.

This is a lengthy article in which the writer maintains that the diagnosis of epilepsy is not made frequently enough in childhood. It must be distinguished from spasmophilia, infectious convulsions and the convulsions following breath-holding. Epilepsy may occur without a change in the mentality, but its development renders the prognosis less favorable.

In traumatic epilepsy, intelligence defects may occasionally disappear.

GERSTLEY, Chicago.

TEN CASES OF ENCEPHALITIS POSTVACCINALIS: FURTHER COMMUNICATIONS ABOUT THE TREATMENT OF ENCEPHALITIS POSTVACCINALIS. J. HEKMAN, Nederl. Tijdschr. v. Geneesk. **2**:4774 (Oct. 12) 1929; 5227 (Nov. 9) 1929.

The author described several cases of encephalitis postvaccinalis which occurred in Rotterdam during the time when many vaccinations were made in this town, in connection with the occurrence of "alastrim." In the first article ten cases were reported, eight occurring after primary vaccination and two after revaccination. In all cases the reactions to the vaccination had been strongly positive. In the

cases occurring after primary vaccination the clinical picture was about the same; in the two cases after revaccination, it was different. In the first of the latter cases the symptoms of encephalitis appeared as early as two days after the revaccination, thus much earlier than usual (from nine to twelve days after vaccination). In the second patient, who died, the anatomic changes found on microscopic investigation of the brain were different from those usually found in encephalitis postvaccinalis. As had already been done by some investigators, the author gave the majority of the patients injections of human serum obtained from persons who had been vaccinated successfully at about the same time as the patients. By preference the author made use of the serum of the father or mother of the patient, a serum which was obtained under the same conditions. The serum was given intravenously, 10 cc. from one to three times daily.

In the second article two additional cases are described. In many of cases in which treatment was given, cases which sometimes were very severe, the author received the impression that the serum treatment had contributed in a high degree to the recovery of the patients. His experience prompted him to give the serum also to those patients who came into the hospital with a normal temperature. One case, in which it was impossible to give strictly homologous serum and in which the patient died, the disease had a protracted course and the hyperpyretic temperature, which is frequent in this form of encephalitis, appeared much later than usual. The author therefore had the impression that even in this case the serum played a rôle by lengthening the clinical course, especially since the convulsions disappeared after the first injection.

VAN CREVELD, Amsterdam, Holland.

Diseases of the Eye

HYDATID CYST OF THE ORBIT. PERFORATION OF THE ORBIT AND ESCAPE OF THE CYST THROUGH THE NARES. B. ADAMANTIADÈS, Arch. d'opht. **46**:368 (June) 1929.

The case of a girl, aged 11, is reported. The chief symptoms were exophthalmos of the right eye and paralysis of the right internal rectus muscle. There was no pain and no tumor could be felt. At operation no tumor was found, but a probe liberated some yellowish pus and with it a perforation of the nasal wall of the orbit was found. A week after the operation while the patient was blowing her nose, a large piece of membrane came away. This proved on examination to be the wall of a hydatid cyst.

The author calls attention to the freedom from pain in his case and the possibility of its development after an examination. He could find only one other case in the literature in which the cyst was expelled through the nares.

MARLOW, Syracuse, N. Y.

GLIAL DEGENERATION OF THE OPTIC NERVE, HEREDITARY, PROBABLY CONGENITAL; CENTRAL VESSELS INVOLVED; STRABISMUS. HANDMANN, Klin. Monatsbl. f. Augenh. **83**:145 (Aug.-Sept.) 1929.

The author describes a condition of the disks, resembling the atrophy following a choked disk, but differing from it by a peculiar arrangement of the blood vessels. The patients were mostly children in whom strabismus was noticed at an early age, or since birth. None of them had shown any symptoms of a general disease. Syphilis could be excluded. Rotatory nystagmus was present in some of these cases. Vision varied from 4/18 to amaurosis, and pupillary reaction was present or lacking according to the degree of atrophy of the optic nerve. The disks were sharply defined; their margins and adjacent parts were pigmented and the color was of a pale to grayish green; they were flat but not excavated. The funnel for the vessels was rudimentary, or missing, or in some instances, replaced by a dense central formation, glial in type and of a grayish green. The lamina could not be seen. The central vessels were not discernible, but the peripheral ones of the disks

were enlarged; many of them started at the margin of the disk and took a straight course into the retina; their walls and striation appeared normal; their diameter, especially that of the arteries, seemed reduced. The disks were of the usual size. The presence of an atrophic ring around the disks and pigmentation surrounding it gave evidence that the adjoining retina and choroid were involved. Proliferation of the glia between disk and macula was seen in one case. The remainder of the fundus was always free from changes including retinitis pigmentosa. The lacking reflex in the macula seemed to indicate hypoplasia of the retina.

The condition described remained unchanged during several years' observation, indicating that it was identical with a closed process. Heredity was present in one case in which the fundus of father and son offered the same picture. Only a few other symptoms of degeneration were found in these six cases: asymmetry of the face coupled with a lower position of the orbit on the side of the affected disk and slight ptosis of 2 mm. In another child there was perinuclear cataract, oval pupil of the affected eye and microcornea of 9 mm. diameter of both eyes. The age of four patients ranged between 5 and 10 years; two others were aged 14 and 21 years, respectively. The observations in these cases are distinctly different from those published by Koyanagi, von Hippel, Heine and from those described by Leber under the heading "diseases of the optic nerve on a hereditary base" all of which appeared at a later age; they were caused by toxic or endocrinous influences. Alsberg's case of heredity is still different (*Klin. Monatsbl. f. Augenh.* **79**:832, 1927), as are Behr's (*Klin. Monatsbl. f. Augenh.* **47**:138, 1909), who found numerous signs of degeneracy in his patients. The patients in the author's cases were healthy, with changes limited to the eyes and face.

The author considers his cases as a special type of central glious degeneration of the optic nerve with a typical involvement of the central retinal vessels. He is doubtful whether the condition is hereditary or the result of an inflammation suffered early in life. The former is at least probable in these cases as the same picture is offered as that seen in the case of father and son. The condition seems to have developed at the time of the formation of the vessel funnel which in these cases is replaced by mesodermal tissue. The condition may correspond with a coloboma free from malformation, defects or pitting. Velhagen emphasized that smallness of the disk and other changes of the optic nerve may happen without the formation of a coloboma.

The author, in agreement with Seissinger, presses the importance of exact examinations of the eye in infants and new-born children.

STOLL, Cincinnati.

GLIOMA OF THE RETINA HEALED BY THE ROENTGEN RAYS. P. KNAPP and M. LUEDIN, Klin. Monatsbl. f. Augenh. **83**:279 (Aug.-Sept.) 1929.

Roentgen treatments, as reported heretofore, have resulted in the shrinking of the glioma tumors but not in their disappearance. In three of the forty-three cases reported, the condition may be considered healed within from fourteen months to three years after treatment, although the tumors did not disappear completely. These were the cases of Schoenberg, Verhoeff and Axenfeld. The only case offering full assurance of a permanent cure is that of Heine in which the condition healed after one exposure more than ten years prior to the publication of the case.

The authors report another case in which the tumor disappeared. A girl, aged 1 year, had her left eye enucleated in November, 1922. Microscopic examination showed a typical glioma of the retina. A small tumor, about 2 prism diopters in size, was discovered in the temporal portion of the fundus of the second, right, eye on Jan. 10, 1923. After six radium treatments had failed to bring about a change, roentgenotherapy was resorted to. Seven treatments were given between May 5, 1923, and Feb. 15, 1924. Then the shrinking of the tumor became noticeable. Four more exposures followed between June, 1924, and March, 1925, resulting in further shrinkage. This was observed in May, 1925, simultaneously with some changes brought about by the rays: A portion of the hair of the brow had fallen

out, telangiectasia had developed on the lid and on the conjunctiva of the globe. Fine disk-shaped opacities in the posterior cortical indicated beginning roentgen cataract. The exposures were discontinued; the fundus could be observed until 1927. Discissions of the cataract were done twice. Absorption took place slowly, and discission of the capsule followed. Examination of the fundus revealed the complete disappearance of the tumor; only a discoloration remained resembling a chorioiditic patch, similar to Salzmann's picture of a spontaneously healed glioma in the fifteenth edition of Fuchs' textbook. The vessels, observed formerly on the tumor, had disappeared. No other pathologic changes were seen in the fundus. The field of vision was normal. The telangiectasis were unchanged, the eyelashes had grown again, rather scantily. The cornea and iris were normal.

The authors are convinced that the tumor was a glioma, as one was present in the other eye. They consider it cured by the rays and not by spontaneous healing, as in the cases of Siegrist, Purtscher, Meller, Salzmann and Axenfeld-Sticherling, in which some tumor-like masses remained. (The case of E. V. Hippel, abstracted in *Arch. Ophth.* **1**:254 [Feb.] 1929, may be added). Technical descriptions of the roentgen treatment conclude the article.

STOLL, Cincinnati.

INFORMATION CONCERNING DICTYOMA RETINAE. J. BÖCK, Ztschr. f. Augenh. **69**:17, 1929.

An enucleated eye of a girl, aged 16 years, presented a tumor mass, which seemed to originate in the unpigmented inner epithelial layer of the ciliary body. The histologic examination showed clumps of cells arranged in roset formation, together with bands of glial tissue. Several areas of cartilaginous structure were also noted. This mass did not, however, present other gliomatous characteristics. A survey of the literature revealed seven other similar cases in children from 1 to 8 years of age.

Böck considers this tumor mass a dictyoma, according to the description of Emanuel. He believes it to be different from growths generally originating in the ciliary body. It probably proliferates from a modification of germinal anlage.

YUDKIN, New Haven, Conn.

A LENTOID PROCESS IN A HUMAN MICROPHTHALMUS. FRANZ FISCHER, Ztschr. f. Augenh. **69**:30, 1929.

Fischer describes the presence of a lentoid process in a microphthalmic eye which was removed from a child, aged 15 years. His interpretation of this observation is unusual. He describes the specimen in detail and concludes that the so-called lentoid process which seems to originate from the ciliary epithelium resembles a similar process found in the amphibia. This assumption would lead one to believe that the cells of the ciliary epithelium in the human eye have the power to regenerate lenticular cellular tissue.

YUDKIN, New Haven, Conn.

Diseases of the Ear, Nose and Throat

BACTERIAL STUDY OF HEMOLYTIC STREPTOCOCCI FROM A MASSACHUSETTS OUTBREAK OF SEPTIC SORE THROAT IN 1928. ELLIOTT S. ROBINSON and EDITH A. BECKLER, J. Prev. Med. **3**:225, 1929.

From the bacteriologic study of the outbreak of septic sore throat in Lee, Mass., in July, 1928, it appears that the causative organism was *Streptococcus epidemicus*, the same etiologic agent found by others in previous outbreaks. This organism was found in the throats of a number of patients, in the aural discharge of some and in the blood of one. The milk-borne nature of the epidemic is shown by the epidemiologic evidence presented by Lombard and by the finding of *S. epidemicus* in a cow that had been providing part of the milk consumed by the patients. The

source of the cow's infection remains undetermined and probably undeterminable. By the usual criteria, *S. epidemicus* is of human, not bovine, origin, and it is reasonable, therefore, to suspect a human source. Although there was illness on the farm at a time when the cow might be supposed to have been infected, the epidemiologic evidence is not of itself sufficient to connect this illness with the infection of the cow, and there is not at present bacteriologic evidence to link the two. The isolation of *S. epidemicus* from the throats of patients is not difficult if one is familiar with the colony typical of this organism. Since there may be little hemolysis around the surface colony when grown on a moist medium, it may be overlooked; for the colony does not greatly resemble that of the more usual hemolytic streptococci. Culturally, the strains of *S. epidemicus* obtained during this epidemic appear identical with those isolated during previous outbreaks.

AUTHORS' SUMMARY [ARCH. PATH.].

INNER EAR AND CEREBELLAR CHANGES IN PATHOLOGIC FETAL POSITION. ANTONIN PRECECHTEL, Laryngoscope **39**:421, 1929.

The vestibular organ should be divided, both anatomically and functionally, into two parts; namely, the otolith system and the semicircular canal system. The former system mediates the reactions to position, while the latter responds to the positive or negative acceleration of movement, whether progressive or rotary. It has been shown by various investigators that reflexes due to rotation, such as nystagmus and head deviation, occur in the newly born infant, and by inclining the body in different directions, especially backwards, it is possible to obtain peculiar reflexes of the limbs. These reflexes provoked by the inclination of the body and by progressive movements are of labyrinth origin. As is generally known, the reactions to position are apperception of the vertical and regulation of muscle tonus. The control of muscle tonus has been studied extensively by the school of Magnus and is classed by this school into three groups, namely: (1) controlling of the eye; (2) reflexes regulating posture; (3) righting reflexes. The first of these does not concern this subject, but the other two jointly control the erect posture and walking of man.

From a careful study of these reflexes together with their effect on posture during the early years of life, it is obvious that the postnatal static and locomotive functions are considerably influenced by the vestibular apparatus. The author believes that it is only logical that one ask whether the typical position of the fetus, and possibly even the attitude of the fetus, is likewise controlled by the vestibular apparatus, in view of the fact that the labyrinth reflexes have been detected both in fetuses and immediately after birth. Various theories have been advanced by Aristotle, Simpson, Kristeller, Griffith and others as to what controls the position of the fetus toward the end of pregnancy, but these, the author believes, have all been disproved. On the other hand, he asserts that none of the facts contradict the explanation of the mentioned position by a static function of the fetus itself, a function reflectorily controlled by the organ which has been proved to serve, in conjunction with other reflexes, the purpose of orientation in space. This view offers a uniform regulation of movements and positions in all the periods of life and is compatible with the modern physiologic theory of the kind of regulation, and is also supported by the fact that the vestibular organ is developed at a remarkably early period. Bechtierew has discovered that the vestibular nerve myelinizes long before the cochlear and other sensitive nerves. It has been found by Flechsig and His in examining a 16 cm. fetus that the branch of the vestibular nerve going to the superior semicircular canal was myelinized as far as the ganglion of Scarpa, and the ramifications of the macula sacculi and utriculi were also myelinized at this stage. It was found in a fetus from 18 to 19 cm. long that the cupulae with hairlets were developed, and Minkowski stated that the faculae develop when the fetus is only two months old. Consequently, tonic influence is exercised early on the various muscle groups. The movements of the labyrinth fluid, which is influenced by gravity, prove a specific stimulus for the vestibular nerve. In this

connection it may be stated that the period in which the myelinization of the vestibular nerve is accomplished covers also the stabilization of the normal position of the fetus at the end of pregnancy.

The author attempted to support this static theory of fetal positions still further by clinically examining such cases as showed abnormal position during the fetal period. A considerable number of such cases appear at otolaryngologic clinics, the patients' complaints falling within the sphere of phoniatry. In the cases studied, the author found, besides an anomalous position during the fetal period, static disturbances in the early postnatal years, as evidenced by a retarded power of sitting, standing and walking. This syndrome is sometimes attended by a speech defect, known as audimutitas, and caused by changes in the cerebellum in the region of the lingula. The lingula is one of the structures of the basal stage of the cerebellum, to which the vestibulocerebellar paths directly converge, and it plays a certain part in the movement of the vocal cords.

The author studied six cases with a history of pathologic fetal positions. In two of them histologic changes were found in the inner ear and in the central nervous system; in one the changes were in the central nervous system only; while in the remaining three the brain was not examined, but in two of them changes in the inner ear were found, thus making a total of five cases with pathologic changes, out of the six cases under study. The peripheral changes consisted in a heavy hypotonic degeneration of the neuro-epithelium in the cochlea and in the vestibular apparatus. In addition, one case presented an extensive primary disturbance of the development of the inner and of the middle ear. The changes were either unilateral or bilateral. The central changes affected the medulla, the midbrain or the cerebellum.

The speech disturbances which are frequently associated with the syndrome may be divided into two groups: (1) speech disturbances of those who are hard of hearing and (2) audiomutism. The peripheral changes explain the disturbances of speech based on decreased hearing, while audiomutism is related to functional disturbances of the cerebellum. The changes in the lingula are especially suggestive in these speech disorders, owing to its relation to the movements of the vocal cords.

SNAPP, Grand Rapids, Mich.

TONSILLECTOMY IN THE PREVENTION AND TREATMENT OF RHEUMATISM. LEONARD FINDLAY, JAMES W. MACFARLANE and MARY M. STEVENSON, Arch. Dis. Childhood **4**:313 (Oct.) 1929.

A group of 153 patients were observed for from five to eight years. The authors realize that the group is small, but the results are reported because the patients have been observed closely by one group of persons. Tonsillectomy may render a child less susceptible to rheumatic arthritis but not to chorea. In the cases of arthritis a tonsillectomy may render the heart less liable to attack, but it must be performed before the second attack. Since there is considerable difference in the progress of rheumatic infection limited to arthritis and of that characterized by chorea, it is suggested that possibly two different strains of organism are responsible.

PETERMAN, Milwaukee.

DISTURBANCES OF DIGESTION AND NUTRITION PRODUCED BY ACUTE LATENT OTITIS MEDIA IN THE NURSLING. S. E. BURGHI and CARLOS GIANELLI, Arch. latino-am. de pediat. **23**:629 (Aug.) 1929.

The authors have observed that otitis media in the hospitalized nursling is much more severe and is more commonly followed by grave digestive and nutritional disturbances than is otitis media in private practice in the home.

The latter is manifest, easily diagnosed and fairly easily and certainly cured. The former often is latent, not at all easily diagnosed and ends fatally unless there is major surgical intervention.

The authors find the explanation in the fact that nearly 90 per cent of their hospitalized patients are in a dystrophic or athreptic state on admission. The general immunity of such infants is at its lowest ebb,

The constant recumbent position of the hospitalized infant favors the gravitation of infected material from the throat to the middle ear and the mastoid. The otitis media in these cases is almost symptomless. The authors aptly designate it as an otitis media latent or occulta.

Vomiting and diarrhea are frequent symptoms of the condition and lead to serious dehydration. The authors found the condition in 116 of 310 nurslings. The condition was also found in 80 per cent of the autopsies performed.

Careful dietetic treatment with free paracentesis and early antrotomy have proved the best methods of treatment. The extensive North American literature on this subject has apparently not come to the notice of these authors, as it is not mentioned.

SCHLUTZ, Minneapolis.

LATENT OR UNRECOGNIZED PURULENT OTITIS MEDIA IN INFANCY AND EARLY CHILDHOOD. ENRIQUE PRADA, Arch. españ. de pediat. **13**:275 (May) 1929.

The author gives an interesting review of continental literature on the subject. No American authors are mentioned.

In 80 per cent of autopsies on infants, purulent otitis media or mastoiditis is found.

Dr. Rendin of Lyon found the condition present in eighteen of nineteen infants who died when less than 1 year of age. The organism found generally was pneumococcus, less frequently staphylococcus. In one case the bacillus of Koch was found. This infant had died of tuberculous meningitis.

Sympathetic involvement of the gastro-intestinal tract commonly occurs in these purulent conditions in and about the ear.

Hartman and Pofick were apparently the first to call attention to this relationship, although a medical candidate by the name of Troelsch, in 1860, wrote a doctor's thesis on the subject of latent purulent otitis media in the nursling.

The symptoms of concealed purulent otitis media are more fulminating in the young nursling than in the older child. The fever is higher. There is more vomiting and the loss of weight is precipitate.

Early surgical procedure is the only successful measure.

SCHLUTZ, Minneapolis.

Diseases of the Skin

THE RADIUM TREATMENT OF EXTENSIVE HEMANGIOMAS IN INFANTS. SANFORD WITHERS and JOHN R. RANSON, Am. J. Roentgenol. **18**:326 (Oct.) 1927.

The authors recommend implantation of radon seeds of low content throughout the bulk of hemangiomas. Application of a compression bandage over the growth following implantation aids by partially collapsing the blood spaces. The mechanism is thought to occur through production of endarteritis and fibrosis of the vessels involved by the beta rays. A case of massive hemangioma of the lip and a multiple hemangioma of the vulvae, vagina, rectum and buttocks are reported; there was no scar in the first instance, and slight telangiectasis in the second. A single treatment is used and one seed of from 0.2 to 0.3 millicuries is used for every cubic centimeter of tumor bulk.

STULIK, Chicago.

TWO EXAMPLES OF EARLY CUTANEOUS NEURO-FIBROMATOSIS IN CHILDREN. W. A. ALEXANDER, Edinburgh M. J. (Tr. Med.-Chir. Soc.) **36**:192 (Sept.) 1929.

Dr. Alexander showed boys, aged 5 and 7 years. In one there were brown marks on the skin, and small lumps on the chest just under the skin. These were soft, elastic and painless. There were other subcutaneous nodules and deeper

swellings related to the nerves. The mother of the other child had definite von Recklinghausen's disease; although this boy showed only one suspicious nodule there were many café-au-lait spots on the body. NEFF, Kansas City, Mo.

NEVUS ANGIOMATOSUS WITH ATROPHIC ZONES, NOT PRECEDED BY ULCERATION. H. GOUGEROT and BURNIER, Arch. dermat.-syph. d. lhôp. St. Louis **1**:177 (March) 1929.

An infant, aged 6 months, presented an extensive port wine mark, which was undergoing regression without ulceration. The cleared zones, however, showed atrophy. MICHAEL, Houston, Texas.

COMPARATIVE VALUE OF PROTEIN DIET AND OF EXTERNAL MEDICATION IN THE TREATMENT OF ECZEMA IN INFANTS. J. CATHALA and M. VERMOREL, Bull. Soc. pédiat. de Paris **27**:196 (April) 1929.

The authors present a boy, aged 9 months, who had eczema since the age of 4 months. It began on the face and quickly spread over the entire body. He showed no improvement after a period of treatment with a milk-free high protein diet as recommended by Hamburger, but improved markedly on application of a coal tar ointment to the skin. Examinations of the blood showed a disturbance of the water metabolism seven weeks after the child had been getting the high protein diet, whereas similar blood determinations were normal after the eczema was cured by the use of the coal tar ointment. BENJAMIN, Montreal.

THE TREATMENT OF ECZEMA WITH HYDROCHLORIC ACID MILK. T. SANDELS, Arch. f. Kinderh. **88**:146 (Aug. 20) 1929.

Sandels made functional skin tests on 160 infants and children, and found that 60 per cent of them between the third month and eight year of life showed a hyperirritability of the skin to a 4 per cent solution of formaldehyde. In using Sheer's hydrochloric acid milk this hypersensitivity disappeared in twenty-five of twenty-six cases, and did not return when the administration of the acidified milk was discontinued. In experiments with less readily oxidizable organic acids, such as tartaric acid and alphaisohydroxybutyric acid, the desensitization was less marked, corresponding to the less satisfactory results obtained with these acids in the treatment of eczema. The author believes that these observations explain the efficacy of milk acidified with hydrochloric acid in the treatment for eczema.

SANFORD, Chicago.

Surgery and Orthopedics

ROENTGENOLOGICAL ASPECT OF INTUSSUSCEPTION. HOWARD E. ASHBURY, Am. J. Roentgenol. **18**:536 (Dec.) 1927.

A discussion of the etiology, symptomatology and mechanism of intussusception is followed by case reports and opinions of various observers as to the efficacy of opaque enemas as a diagnostic help. With a few exceptions all are in accord that roentgen examination by opaque enema is, as a rule, the quickest and safest method of locating the point of obstruction in intussusception and frequently visualizes the invagination; that the information gained is of the greatest value, and that its use does not materially delay operation. A few authors were able to visualize lesions by an ingested meal, while a few reported instances of intussusception in which a barium sulphate enema did not show any abnormality. Reduction by enema should not deter the surgeon from opening the abdomen when the symptoms are reasonably conclusive. In chronic intussusception, except in complete obstruction, examination by ingested meal can be made with relative safety. STULIK, Chicago.

PROGRESSIVE STRAIGHTENING OF DEFORMITIES OF THE KNEE IN THE CHILD. DUCROQUET, JR., Bull. Soc. de pédiat. de Paris **27**:201 (April) 1929.

The author reports a series of cases of deformities of the knee in children, of genu valgum and genu varum types, due to rickets, which he corrected by the use of plaster spicas made over padding to include the space through which the leg would have to be moved in order to effect the necessary correction; over this space the plaster was cut out and the padding removed so as to leave an open space. This space was gradually filled in with more and more cotton padding to exert more and more pressure in the direction required to straighten the knee. In cases in which he did not use plaster he devised a brace apparatus fitted with a screw over a lever which allowed him to use the same principle of gradually exerting pressure in the direction necessary to straighten the knee. All of these patients were cured in less than three months. The author recognizes the well known fact that some rachitic deformities spontaneously straighten themselves as the rickets is cured by the administration of sufficient amounts of antirachitic vitamin, but he believes that one should correct the deformities at the beginning of the antirachitic therapy so that the bones attain their normal density after being straightened, rather than cure the rickets and at a later date try to correct the deformities. He treated a hundred patients with rachitic genu valgum and genu varum by the foregoing methods and cured all of them in from six weeks to two and a half months. He also used the same methods in the treatment for deformities of the knee as a result of osteomyelitis of the lower end of the femur and the upper end of the tibia, tuberculosis (without ankylosis) and infantile paralysis—all with good results. The article contains numerous photographs of children before and after treatment, and sketches to illustrate the plaster spicas and the screw type of apparatus used.

The advantages of the method are chiefly the elimination of any operative procedure and anesthetic and doing away with the necessity of removing the plaster repeatedly to apply a new spica each time in the "stages" until a cure is reached. Roederer, in discussing the paper, draws attention to some disadvantages: The method is good only in skilled hands and is not for general use; it is difficult to limit the action of the force applied to any particular point and there is too much pull on the ligaments, especially of the knee (the author refutes this by pointing out that in no case was there any abnormal movement of the knee-joint after treatment); the child has to be seen often; and rachitic children should have their skin exposed to the sun and fresh air as much as possible.

BENJAMIN, Montreal.

FOUR CASES OF ACUTE SUPPURATIVE ARTHRITIS OF HIP-JOINT. F. CROOKS, Proc. Roy. Soc. Med. **22**:1523 (Oct.) 1929.

Four cases of acute suppurative arthritis of the hip joint were reported in patients aged 7 years, 2½ years, 8 years and two years and seven months, respectively.

WILLIAMSON, New Orleans.

TREATMENT FOR EMPYEMA IN THE CHILD: THORACOTOMY WITH RIB-RESECTION. MARTINEZ VARGAS, Arch. españ. de pediat. **13**:321 (June) 1929.

Treatment for empyema must be exclusively surgical. As much of the purulent fluid as possible must be withdrawn with the needle.

If the pus reforms rapidly, the author recommends operative procedure and prefers thoracotomy with rib resection. The author is opposed to closed irrigation.

If the pus bubbles freely from the wound it argues for vigorous lung action. In this case, the author opens the wound freely and resects part of one rib. If the pus issues in the form of sanguinolent fluid, it indicates very recent pulmonary inflammatory process.

The opening in the pleura should be very small, and the escape of the fluid slow. The heart is allowed to assume its normal position gradually. Too rapid evacuation of the fluid provokes attacks of syncope.

If the pus issues thick and without bubbling, it indicates lung retraction according to the author. Expansion will be difficult and slow. In such cases the author recommends resection of part of two ribs. Incision is best made in the region of the eighth or ninth rib. The cavity is irrigated with surgical solution of chlorinated soda.

The author follows the same procedure in tuberculous purulent pleurisies. In serofibrinous pleurisies aspiration will often suffice, along with the use of small quantities of autogenous vaccine.

SCHLUTZ, Minneapolis.

Miscellaneous

POPPIS: A CODE WORD FOR THE APPROACH TO DIAGNOSIS IN CHILDHOOD. JACOB SOBEL, New York State J. Med. **29**:1146 (Sept. 15) 1929.

As the medical student used code words and rhymes to remember cranial nerves, anatomic relationship and other problems, so it is suggested that the code word "poppis" will assist the attending physician to remember the various conditions that may affect a sick child. The letter p recalls pharyngitis; o, otitis and osteomyetitis; p, pneumonia, pleurisy, pericarditis, pertussis, and so on.

AIKMAN, Rochester, N. Y.

A STUDY OF NEGRO INFANT MORTALITY. A. L. STOUGHTON and M. GOVER, Pub. Health Rep. **44**:2705 (Nov. 8) 1929.

In every area studied, the negro infant mortality rates were higher than those for white infants. The lowest rates were in the rural south, and the highest in the southern cities. The mortality rate is higher for negro infants for all diseases except diphtheria, meningitis (epidemic), erysipelas and scarlet fever. The greatest mortality was from unknown causes, respiratory diseases, gastrointestinal conditions and tuberculosis. The highest ratio is between the fifth and tenth months. High mortality during the first month is due to premature birth and congenital debility.

SANFORD, Chicago.

THERAPEUTIC USES OF CARBONIC ACID. H. WHITRIDGE DAVIES, Edinburgh M. J. **36**:385 (July) 1929.

This paper by Professor Davies of the Department of Physiology, University of Leeds, was awarded the Parkin prize by the Royal College of Physicians, Edinburgh, in 1929.

Davies reviews the accumulating knowledge that has changed the conception of carbonic acid as a waste product of metabolism to one of extreme importance in governing circulation of the blood, in the regulation of breathing and in the maintenance of the acid-base equilibrium. Such a powerful physiologic agent would be expected to have valuable applications in therapeutics.

The therapeutic applications are as yet only faintly realized. Carbonic acid is the natural physiologic respiratory stimulant, is therefore the safest and has been found to be the most efficacious. The author states that carbon dioxide inhalation causes an increased respiratory response in conditions of impaired general circulation (such as mitral stenosis) and in nongaseous acidosis. Respiratory failure, depression of the respiratory center from narcotic poisoning, volatile poisoning by methyl alcohol, by sulphureted hydrogen and by carbon disulphide are some of the indications for the use of carbon dioxide.

The use of carbon dioxide in anesthesia is of great value in controlling the amount of pulmonary ventilation, so that absorption as well as elimination of ether is accelerated, thus requiring a smaller total amount of ether. Rapid deetherization after anesthesia, lessening of postanesthetic nausea, vomiting, collapse and pulmonary

complications will result from the administration of carbonic acid. Davies and Christie found undeniable proof of the value of carbon dioxide in anesthesia in its prevention of severe prolonged vomiting.

Carbon dioxide is of great value in treating patients for carbon monoxide poisoning, in shock and collapse, and in the treatment for alkalosis. Professor Davis states that the world is greatly indebted to Yandell Henderson of Yale University for the life-saving methods which he brought out, especially in anesthesia. (Henderson has also emphasized the value of carbon dioxide and oxygen, 1:20, for stimulation of the respiratory center of asphyxiated new-born infants.

Davies refers to another article for his description of the method of administration. For prolonged use he advises a cylinder, a fine adjustment-regulating valve, a flow meter and a suitable mask.

NEFF, Kansas City, Mo.

REPRESSION OF JUVENILE CRIMINALITY. VANDERZYL, Rev. internat. de l'enf. **7**: 183 (March) 1929.

In comments on juvenile delinquency and its control in the Netherlands, the author makes an earnest plea for a better understanding of the factors involved and for a wider appreciation of the newer and more logical objective, reclamation. The old idea of punishment for crime, in the case of adolescents, is gradually giving way everywhere to correction and education; society is concerning itself more with the sources of delinquency and the development of suitable measures to combat them. Ordinances designed to improve the social status of the young, by regulating the hours of labor, by enforcing school attendance, by providing salubrious lodgings and by prohibiting employment of minors in the liquor traffic, will aid materially in reducing the number of children annually recruited in the armies of vice and crime. For those already delinquent, a distinction must be made among those guilty of a first offense and those who are habitually before the police. The former are readily reclaimed in most instances; the others present a problem which can best be solved by the combined efforts of the alienist and the psychologist. Juvenile courts would profit greatly through such consultations; suitable cases could be sent to a behavior clinic and the more incorrigible ones to a detention home, which in any event should be the substitute for an actual penal institution. In this correctional center, education will frequently obviate the necessity for disciplinary measures; physical disabilities are adjusted wherever this is possible, and individual management substituted for mass training. Vanderzyl expresses his belief that the results of this radical departure in the treatment for delinquency will more than compensate for the initial expense incurred.

AMESSE, Denver.

SOME NECESSARY REFORMS IN MILK DISTRIBUTED BY CHARITY. G. VARIOT, Progrès. méd. **44**:1961 (Nov. 9) 1929.

Variot stresses the necessity of sterilizing cow's milk at 108 C. instead of the customary 100 C. This is particularly to increase the digestibility of the milk. Artificial milks, particularly condensed milks, are better tolerated by the newborn than is cow's milk. For this reason these milks are better for the average charity patient than cow's milk.

SANFORD, Chicago.

A FUNCTIONAL AND RESISTANCE TEST OF THE KIDNEYS. K. KUNDRATITZ, Ztschr. f. Kinderh. **47**:261, 1929.

By the intramuscular injection of 2.5 cc. of sterilized milk in children who have clinically healed inflammation of the kidneys there is the possibility of a functional and resistance test. It gives a sure prognosis and tells whether the kidney is not only functionally but morphologically healed. On the basis of the test one can judge to a certain degree whether the kidneys in a patient are capable of withstanding a projected operative procedure, such as a tonsillectomy, or whether a relapse is to be feared.

EMERSON, Boston.

THE FAVORABLE RESPIRATORY ACTION OF CORAMIN. H. HEIDEMANN, Ugesk. f. laeger **91**:733 (Aug. 29) 1929.

In patients suffering with bronchial asthma excellent results were obtained with coramin. One or two ampules are given intramuscularly or intravenously; smaller doses are used for children. The drug gives relief from expiratory distress and promotes expectoration.

No toxic effects have been observed, nor has tolerance for the drug increased.

SCHLUTZ, Minneapolis.

THE TENSION RELATIONS OF THE SPINAL CORD IN LORDOSIS AND KYPHOSIS AND THEIR SIGNIFICANCE IN THE TREATMENT OF ACUTE POLIOMYELITIS. FRANZ BECKER, München med. Wchnschr. **76**:1547 (Sept. 13) 1929.

In the acute stage of poliomyelitis, the patient is more comfortable when the spine is held in lordosis. According to Lange, lordosis produces relaxation of the spinal cord, whereas kyphosis produces tension. Becker examined cadavers at various ages and confirmed this explanation. He exposed the spinal cord and severed it at the level of the seventh cervical and first lumbar vertebrae. In a child, aged 5 years, he found that holding the vertebral column in kyphosis caused the cord at the cervical level to separate for 20 mm., whereas in the lordotic position the cut ends overlapped for 3 mm. Similar changes were observed at the lumbar level. Infants, older children and adults showed equally striking differences. Becker strongly recommends placing the patient in lordosis in the treatment of acute poliomyelitis.

BRAHDY, Mt. Vernon, N. Y.

INFECTION OF THE MENINGES FOLLOWING LUMBAR PUNCTURE. L. DRÜNER, München. med. Wchnschr. **76**:1594 (Sept. 20) 1929.

Drüner calls attention to the possibility of infecting the meninges by lumbar puncture. He recalls a case in his own experience in which, even after careful asepsis of the skin, meningitis followed lumbar puncture. Fortunately, the patient recovered. To avoid repetition of such occurrences, he now makes a small incision in the skin through which he inserts the puncture needle.

BRAHDY, Mt. Vernon, N. Y.

THE TWINNING PROBLEMS OF SCHIZOPHRENIA. J. LANGE, Wien. klin. Wchnschr. **42**:1213 (Sept. 19) 1929; 1247 (Sept. 26) 1929.

The author calls attention to the known close resemblance between single ovum twins; e.g., identical blood-grouping, similar muscle tone, and almost identical finger prints. He shows in this article that if one single ovum twin develops schizophrenia, the other in all likelihood will do so; and that consequently this condition is due to determinants present in the germ plasm.

Luxemburger's collected data on 16,000 persons included 6,443 with schizophrenia; there were 211 normal twins, and 106 with schizophrenia; i.e., among 60.8 patients with schizophrenia there was 1 twin, and among 55.8 normal persons, 1 twin. Since twins do not die earlier than other persons, the similar ratios indicate that twinning per se does not cause schizophrenia. Study of the 106 schizophrenic twins showed 33 persons who were certainly double ovum twins; in no instance did the partner have schizophrenia. In the 17 cases of certainly single ovum twinning, 10 partners had schizophrenia, 3 probably had, and 2 were peculiar.

The onset of the psychosis in the partners often occurred within a few days, even when the twins had lived separately. The content of the psychosis was frequently similar. Different environment and intercurrent organic disease may modify the psychosis in one partner. The more highly educated partner tends to develop the psychosis earlier.

CLAUSEN, Rochester, N. Y.

PHOSPHATURIA, RICKETS AND TETANY AS MANIFESTATIONS OF INADEQUACY OF THE BRAIN. J. AIGINGER, Wien. klin. Wchnschr. **42**:1217 (Sept. 19) 1929; 1252 (Sept. 26) 1929.

According to the author, persons suffering from "phosphaturia" look well, have weak stomachs, feel well only in summer, sleep and eat too much, do not care to smoke, have disturbed respiratory rate and volume, and excrete in the urine an excess of calcium. All present signs of an earlier rickets. The author attributes the disorder to an irritability of the respiratory center dependent on lack of inhibition from vegetative centers in the mid-brain, and to a consequent carbon dioxide acidosis, with resultant mobilization and excretion of calcium from the body. He has found that training these patients to breathe properly will give relief from symptoms.

The auther discusses at length the possibility that upset of the vegetative centers in question may play the determining rôle in the causation of rickets, tetany and Swift's disease ("Feer's disease," he terms it).

This ingenious hypothesis ought to stimulate experimental work. In the present article nothing but the hypothesis is presented.

CLAUSEN, Rochester, N. Y.

CEREBELLAR HEMORRHAGE RESULTING FROM PLAY. H. R. KROGSGAARD, Ugesk. f. laeger **91**:732 (Aug. 29) 1929.

A girl, aged 7, had played in a strenuous game twenty hours before the onset of symptoms. One hour after she experienced pain in the back of the neck and vomiting, she became irrational and finally comatose. Ten hours later she was dead.

Autopsy revealed a cavity the size of a green walnut, filled with sanguineous fluid and clotted blood. There was also sanguineous fluid in the fourth ventricle.

The length of the interval before objective symptoms appeared is explained by assuming that there was a slowly increasing hematoma which had to attain a certain size before disturbances appeared.

SCHULTZ, Minneapolis.

PROBLEMS CONFRONTING THE JUVENILE COURTS OF GERMANY. LISZT, Rev. internat. de l'enf. **8**:683, 1929.

A federal statute establishing the juvenile court has been in force in the German Republic for six years and, although frequently amended, seems to be functioning well. Extraordinary powers are delegated the judges in matters concerning the disposition of young criminals, ranging from a simple warning to probationary surveillance, reformatory training and imprisonment for periods up to ten years. The courts are permitted to suspend criminal procedure in any case in which disciplinary and educational measures may be substituted.

In 1927, 30 per cent of all cases of juvenile delinquency were handled outside the jurisdiction of the court, while 40 per cent of these delinquents were given small fines or conditional sentences. A close liaison between the judiciary and the staff of social workers is maintained through the Children's Bureau (Jugendamt); private agencies cooperate in many places to the extent of undertaking the care and education of these wards of the court. They also supervise in part the management of delinquents over 18 years of age who do not come under the jurisdiction of this particular authority. Children brought up as witnesses in these cases, especially in sex offenses, require unusual tact and discernment in handling; the moral risk is apparent and the Children's Bureau is frequently called to appraise the value of their testimony. It is felt, in the light of these six years of initiatory regulation, that only an experienced personnel can carry out the spirit of the enactment. At the conference on juvenile courts, held in Stuttgart in 1927, this conclusion was voted unanimously. To this end, classes are being formed for the instruction of volunteer workers, and even for magistrates, continuing in some quarters from nine to twelve months. As in other countries,

particularly the United States where courts of this character originated, it has been shown that juvenile delinquency has its origin not so much in heredity as in unemployment, bad housing conditions, poverty and the inevitable demoralization resulting from a drab environment. In Berlin, the institution of club life for the unemployed has produced, in spite of the increase in the number of idle youths, a marked reduction in juvenile crime. The problem of the foreign delinquent is difficult to solve; expulsion is unsatisfactory and, in certain cases, inhuman. Cooperation among the magistrates of the International Union of Juvenile Courts will doubtless provide relief.

AMESSE, Denver.

Society Transactions

PHILADELPHIA PEDIATRIC SOCIETY

Stated Meeting, Nov. 12, 1929

RALPH M. TYSON, M.D., *President, in the Chair*

A CASE OF THROMBO-ANGIITIS WITH A CLINICAL PICTURE SIMULATING ACRODYNIA. Presented by DR. E. L. BAUER and DR. F. W. KONZELMANN.

An infant, born on April 14, 1929, after a normal delivery, was subsequently fed a pasteurized milk formula containing dextrimaltose. On May 11, she developed an acute rhinitis and bronchitis accompanied by a rash which was thought to be measles. She cried, as if in pain, and gnawed her fingers but never attempted to pull at her hair. Her weight gradually diminished. Eleven days later a pink blush was seen on the hands and the feet, and the finger tips became a very deep red.

The patient, seemingly in great pain, was admitted to Jefferson Hospital on May 26 suffering from marked emaciation and photophobia. There was a seborrhea of the scalp, and the nose was a distinct pink. A deep pink color appeared on the wrists and extended over the hands and fingers, gradually becoming darker, so that the fingers were a deep crimson. The thumbs were not so markedly affected. A similar but less marked process appeared on the feet and toes. Pulsation of the radial and dorsalis pedis was barely palpable. Physical examination showed nothing else of importance. Bronchopneumonia developed, and the child died on June 5, twenty-five days after the first appearance of the symptoms.

While in the hospital, the patient's temperature ranged between 101 and 103 F. The blood count showed 44,100 leukocytes per cubic centimeter of blood, and of these 58 per cent were polymorphonuclears and 33 per cent mononuclears. The Wassermann reaction was negative. The urine contained albumin but no blood or casts.

At the time of necropsy, the discoloration of the hands and feet was marked; the fingers were necrotic and dry. A chronic inflammatory process accompanied by thrombosis was found in the coronary vessels, celiac axis and renal arteries. The digital plantar arteries were completely fibrosed. Subacute pericarditis, interstitial bronchopneumonia, focal necrosis of the spleen, suprarenal and liver and renal infarction were accompanying lesions. Sections of the skin of the toes showed a moderate keratosis and a marked fibrosis of the stratum corium. Examination of the brain was not permitted. Cultures of the skin and heart's blood showed a gram-positive bacillus and coccus. The latter predominated. Accidental death of the animals inoculated with these cultures prevented further bacteriologic studies.

The autopsy observations were indicative of a chronic infectious process, and considering the age of the patient, it is not unlikely, a prenatal infection. Since the clinical symptoms resemble to some extent those of acrodynia or Swift's disease, the authors believe a more thorough investigation of the peripheral vessels should be carried out in those cases of acrodynia that come to autopsy.

DISCUSSION

DR. ARTHUR M. DANNENBERG: Dr. Bauer and Dr. Konzelmann must be congratulated on their excellent study of this case. Granting that the evidence points to infection and knowing that most of these patients without infection fare well, how is it that the majority can recover? I am questioning the diagnosis of acrodynia as I see it. I should like to ask if there were any nerve studies made.

I think that those would give us the real information. An exhaustive report from the Mayo Clinic shows definite degeneration of the nerves to the cord and up the cord and involving at times the basal ganglions. While I should like to agree with the diagnosis of acrodynia, I feel that this child may have had a generalized septicemia. I have had the opportunity to see children with marked cyanosis of the fingers due to a micrococcus infection.

DR. EDWARD L. CORSON: It is a very curious observation that Dr. Bauer and Dr. Konzelmann have brought to our attention. The history of the case, other than the unusual age of the patient and the unusually early infection, certainly suggests acrodynia. When one looks at the photograph of the cadaver, one is struck with the thought that the fingers are so dark that they look to be either hemorrhagic or gangrenous. It is unusual in a case of acrodynia to see such a marked discoloration. The microscopic sections make it more reasonable to explain the appearance of these fingers by the more or less obliterative arteritis present. I should like to know if there were any examinations of the nerves, and if so, was degeneration a pronounced feature?

DR. EDWARD L. BAUER: This child was presented to me at the Jefferson Hospital with the picture that Dr. Konzelmann has outlined to you, and I was very careful to see that the data presented were as full as we could obtain under the circumstances. The picture impressed me as one of acrodynia. I had several cases in the ward, and from the clinical picture in this case, there was nothing to make it appear different from the others, except the fact that the patient was so extremely ill and the progress toward death was the only part of the picture that I had not seen before. Had the child been buried without an autopsy, those who saw her with me, as well as myself, would have been clearly convinced from the clinical side that we had had a death from acrodynia, so certain was the picture. The pulse rate was variable but always rapid.

As the pictures were not colored photographs there is exaggeration of the discoloration. In the hands, the pinkness does not show up over the wrists as in the living subject.

DR. F. W. KONZELMANN: Studies were made of the peripheral nerves in the section of the toe, and they showed neither degeneration nor inflammation.

CAUSES OF ILL HEALTH OF CHILDREN BORN AFTER POSTCONCEPTION PELVIC IRRADIATION. Presented by DR. LEOPOLD GOLDSTEIN.

This is a study of the causes of the ill health of children born of women who were subjected to radium therapy or roentgen irradiation for pelvic disease during pregnancy. The data were obtained from a previous review of the literature and personal letters from the authors who had observed cases of ill health in children after maternal irradiation.

Seventy-six children were born of 107 women irradiated during gestation. Of these children, 39 (51.3 per cent) were unhealthy and 37 (48.7 per cent) were healthy. Any child was considered unhealthy or defective who was stillborn or born prematurely, who was abnormal or deformed at birth, who later presented any pathologic condition whatsoever, or who had died prior to the time of this report. All of the pregnant women were treated for various pelvic and other pathologic conditions, and in many instances were given very large doses of irradiation.

All possible etiologic factors for the child's ill health were studied and weighed in order to determine the rôle played by the irradiation in the cause of the defects. Such factors as maternal health prior to irradiation and during pregnancy, maternal age, hereditary influences, circumstances of labor and prematurity were analyzed in detail. The cause of the ill health of 10 of the 39 children, born after postconception maternal pelvic irradiation, was explained on the basis of influences other than irradiation. Two of these 10 children were microcephalic idiots, 7 were stillborn or died shortly after birth, while 1 child died from intussusception at 2 years of age. The ill health of the remaining 29 children (38.1 per cent) could not be attributed to the influences investigated and was therefore ascribed

to the effects of the irradiation, since this was the only influence common to all of the children. Twenty-one children exhibited mental or nervous disturbances, 8 presented other abnormalities of function or structure. There were 17 microcephalic children in the group of children with cerebral defects.

The large number of grave malformations appearing in the children born after postconception irradiation, the uniformity of these deformities (chiefly microcephaly and other mental defects) and the infrequency of microcephaly in the general population (1 in 10,000 or more births), all strongly indicate that there is a distinct relationship between postconception irradiation and the occurrence of mental defects in children born after such irradiation.

DISCUSSION

DR. RALPH M. TYSON: At what time during pregnancy was the irradiation carried out?

DR. LEOPOLD GOLDSTEIN: In most cases, the women were irradiated in the first two or three months of pregnancy; in one case the mother was irradiated in the fifth month for cancer of the cervix. Her child is now 12 years of age and is an imbecile.

PHYSICAL MEASURES OF GROWTH AND NUTRITION. Presented by RAYMOND FRANZEN, PH.D.

General estimates of nutritional status by qualified physicians were analyzed to determine the accuracy of clinical judgment and the factors which are used. It was found that the agreement between ratings of nutritional status was too small to endorse this form of measurement, nor did an analytic rating scale of forty-six items improve the ratings satisfactorily. The items of such a scale in greatest agreement with total judgment are those dealing with amount and quality of subcutaneous tissue and muscle. The composite of twelve objectified measures agreed more closely with the ratings of any physician than this physician agreed with his colleagues. There was a very wide disagreement in the emphasis bestowed by physicians on each of the twelve anthropometric traits. The main emphasis in judgment made by physicians is on weight and muscle size when allowance has been made for skeletal dimensions. The physician wants to use subcutaneous tissue but fails to do so. None of the physicians whose judgment was studied made the proper allowance for skeletal dimensions.

Factors which account for the individual differences in weight of children other than age were thoroughly studied. The material presented thus far has given consideration to five possible methods of estimating the degree to which the nourishment of a child is satisfactory. These five are: (*a*) actual weight minus the weight to be expected from height; (*b*) actual weight minus the weight to be expected from height, bisacromial width, chest dimensions and width of hips; (*c*) actual upper arm girth minus the upper arm girth to be expected from height, chest dimensions and width of hips; (*d*) actual calf girth minus the calf girth to be expected from the height, chest dimensions and width of hips; (*e*) actual amount of subcutaneous tissue over the biceps minus the amount of subcutaneous tissue over the biceps to be expected from height, chest dimensions, width of hips and bisacromial width.

Arguments which influence the author to advise against any height-weight determinations are as follows: Individual differences in chest dimensions and hips and more important than height as determinants of variations in weight. Expecting more weight for tall children than for short ones (as we do by use of height-weight tables) penalizes tall children unduly in regard to weight which is associated with girths. Correlations of weight for a given height with girth residuals and with subcutaneous tissue residuals are low. If girth and subcutaneous tissue in terms of body build measure aspects of malnutrition, then weight-height determinations are not measures of the same aspects. It seems impossible that weight for a given height should, to any large extent, measure some aspect of

nutritional status not apparent in the condition of muscles and subcutaneous tissue. Accordingly, weight-height ratios measure mainly developmental factors not associated with nutrition.

The reasons for recommending the use of the actual amount of subcutaneous tissue over the biceps, minus the amount of such tissue to be expected from five skeletal measures, are:

1. It is the accepted opinion of the medical profession that the amount of subcutaneous tissue is an element in nutritional status. Whenever a child is considered as totally satisfactory he is sure to be called satisfactory in this quality also and vice versa.

2. Nevertheless, the amount of subcutaneous tissue does not play a part in their actual judgments. Children who are actually unsatisfactory in this quality as measured are often called satisfactory totally.

3. The multiple correlation of skeletal factors with this quality is between 0.5 and 0.6, which is low enough to insure very large residuals.

4. Subcutaneous tissue residuals have a low correlation with the girth residuals, and therefore may be considered as valuable additions which do not in any way duplicate the girth residuals in significance.

5. Differences in the amount of subcutaneous tissue over the biceps represent differences in the amount of subcutaneous tissue in other portions of the body.

DISCUSSION

DR. LOUIS C. SCHROEDER: I make my living practicing medicine, and the problem of diagnosing why a child is 10 per cent underweight comes to me nearly every day. I was one of the fifty-seven physicians who served in the experiment about which Dr. Franzen told you, in which there was such a very remarkable disagreement. I shall try to bring to you a clinical view of the diagnosis of a state of nutrition. I use height and weight tables in spite of the fact that I know the defects in them. The assumption or assertion that nutritional status cannot be diagnosed by any measuring device is wholly without meaning. There never has been any measuring device that would identify malnourished children and there probably never will be one, but by a combination of what we know and by placing everything else in agreement we can judge the state of nutrition.

Many differ as to what constitutes a state of nutrition. When we do away with the disagreement concerning the term nutrition, we shall be a long way toward evolving a definition. Let us examine the conditions under which we, as physicians, examined the children in Dr. Franzen's experiment. They were not children in our private practice; we had no family history or knowledge of any familial tendencies. We did not know of any endocrine dyscrasia, and we had the short space of half an hour to tell the nutritional status. No wonder there were differences among ourselves. We had correlations as low as 40 and the highest 85. Why did we disagree so wholly among ourselves? Some do not like children too fat, others dislike skinny children. We are not agreed as to what are the objective signs of nutrition. Training, personal biases and the ambiguity concerning the term nutrition were responsible for the low correlation.

Biologically and physiologically, nutrition is the sum of the processes that are the result of the ingestion and utilization of food. For many physicians this is too limited, too narrow an interpretation to apply to human beings. We want to agree on what we mean by nutrition and not confuse it with physical defects. We are not considering things that result from nutrition nor things that cause malnutrition. To diagnose properly nutritional status, functional or organic disorders must be considered apart. Not until it is universally recognized that it is desirable to have a content of knowledge concerning the nutritional status of children, which deals primarily and chiefly with food and food habits, rest and personal hygiene, will children be specially judged from this nutritional standpoint. Growth proceeds in two ways. First, there is the result of living in a certain environment, eating a certain amount of food and getting a certain amount of sleep. If we bear this

in mind and think of attaining a certain structure as being primarily the result of the impulse to grow which is inherited from parents, then at once it becomes apparent that using height alone as a measure of nutrition is utterly fallacious. The inherent impulse in a child of small parents, certainly for a time, is going to limit its growth; that is doubtlessly true of its weight, the distance between the trochanters, and for the depth and breadth of chest. When you think of growth in that fashion, how much out will you be when you consider height alone as a measure of growth?

If growth leads to a certain skeletal frame, properly covered with normal muscle and subcutaneous tissue, nutrition may be judged by the manner in which this is accomplished. Logically, it follows that the amount and quantity of muscle and subcutaneous tissue in relation to the entire skeletal frame, and not to one dimension of it, will give us an index of the nutritional status. Criteria of skeletal builds, of girth of muscle and thickness of subcutaneous tissue in all periods from infancy to adult life are needed. With these criteria it should be possible to approach the problem of diagnosing a state of nutrition, secure in the knowledge that the problem is recognized clearly. If these hypotheses are correct, then the proper application of these criteria to groups of children should come closer to diagnosing nutritional status as an entity than the judgment of any one physician or the use of any series of objective judgments. Dr. Franzen and his associates' work apparently proves that this is true. It does not solve the problem of the asymmetrical development of certain children, nor does it take out of the hands of physicians the necessity of deciding what an unusual deviation has come from or what form of treatment is necessary. It points the way to a sound scientific consideration of the problem of nutrition in childhood and offers a measuring device that will undoubtedly find wide use and an ever increasing value.

DR. HOWARD CHILDS CARPENTER: It does seem as if we have been in dire need of further help in determining nutritional status. We have been forced to use height and weight because of our inability to know what other measurements were of most value. Some of us have felt the necessity of using functional tests as well as objective tests and measurements. For instance, tests which in addition to circumference of the chest might include vital capacity or such a functional test as the grip. They have not been treated in this particular discussion, but I do think they are helpful in determining the state of nutrition. The emphasis placed on hip measurements is of particular interest to me because it is one which I fear I have almost entirely overlooked. My own reaction to this work in connection with medical students and interns has been that in their examinations most cursory attention has been paid to nutrition. Their standard is extremely low, much lower than it should be. They are in great need of knowing what a healthy, normal child with a good state of nutrition looks like.

DR. BATSON: It seems to me that the problem that we are interested in is knowing whether this child is going to proceed in an orderly fashion in his development to the adult type. Nutrition has undoubtedly a part in this development, but until the anatomist or anthropologist can tell us more about the adult types and their child progenitors, I am sure we are going to have a hard time to determine whether any particular child is developing properly, because we have in addition to anatomic claims, certain physiologic claims which go with each particular type. In addition to this most valuable work which we have heard presented, it would be most useful to know something about the way this height, breadth and depth is to come about, the form of the skeleton as well as its measurement. We are not interested in the weight of a child any more than has already been pointed out, but we do want to know if the child is going to proceed in an orderly fashion of developmental stages to reach the adult normal for his type.

DR. JOSEPH STOKES, JR.: I have been interested in Dr. Franzen's work for the past two years, particularly as regards the study of identical twins. I have had a number in my practice and I have been watching them particularly as far as nutrition is concerned. I have taken measurements of calves, biceps, triceps, etc., and there has been much variation depending on food intake and methods

of life. Their bony skeletons have been quite similar. I have been searching for a couple of twins who have been separated from early life so as to obtain comparative measurements. I have wondered whether Dr. Franzen may have some data concerning this question.

DR. RAYMOND FRANZEN: We are speaking first of actual dynamic growth factors rather than just actual measurements in themselves. We do not classify by type. We take measurements of hips, chest breadth, chest depth and standing height, but never sitting height; in addition, we take weight, muscle factors, size of calf, biceps, deltoid, amount of subcutaneous tissue over triceps, biceps and calf. To find whether a child is off the normal scale, we can compare a child unlike him in hips but like him in all other respects. This child has a deviation in hips more than that one. If we can find ten children like him in other ways, we are getting close to a symmetry, and also close to what we are looking for. We are taking each characteristic in itself and comparing it to any group of the others. Type alone will not do. Our observations show that we have to use each quality separately. Tables for children aged 10, 11 and 12 are available, and tables down to 6 years will soon be available. We have no data on identical twins to date. Our groups consist of normal school children if we exclude endocrine disorders.

CHICAGO PEDIATRIC SOCIETY

Clinical Meeting, Nov. 19, 1929

MAURICE L. BLATT, M.D., *Chief of Staff, Presiding*

SOME UNUSUAL CASES OF TUBERCULOSIS. Presented by DR. C. K. STULIK, JR.

CASE 1.—A boy was admitted to the hospital on Dec. 20, 1928, with a right otitis media, bronchopneumonia and meningismus. The white cell count varied between 20,000 and 30,000. The Mantoux test on three attempts gave negative results. The chest showed complete consolidation from the bronchopneumonia, with definite cavitation. The spinal fluid (Pandy) was positive, with 76 mg. of sugar and 210 cells, principally lymphocytes. Wassermann and Pirquet tests gave negative results. The disease ran a long, septic course, simulating a tuberculous septicemia.

The child was treated with ultraviolet irradiation, and was sent home after about six months. At the time of presentation he was back for a recheck. The Pirquet test was still negative, but the Mantoux test was positive. The report from the roentgenologic department was that the chest was "healthy" and, as could be seen from the films presented, the last picture showed disappearance of the cavitation.

CASE 2.—A little girl came to the hospital with an acute infection of the upper respiratory tract, with a possible abscess in the region of the clavicle and abscess-like formation in the right tibia. It was thought that we were dealing with pyemia and septicemia, with multiple abscesses and possibly beginning osteomyelitis. Repeated roentgen examination and blood cultures were negative. The Mantoux test became positive in forty-eight hours, and the roentgenograms showed a condition not at all compatible with the initial diagnosis of septicemia. There was a progressive condition in the chest which resembled epituberculosis. Physical examination at the time of presentation showed nothing but decreased resonance in the upper part of the right side of the chest, at the site of the patchy area in the roentgenogram.

CASE 3.—The roentgenograms presented were from a case of spinal bifida occulta, and showed separation of the lateral bodies of the entire dorsal spine. There was a large tumor mass in this region and a gradually progressive spasticity of the lower extremities showing some deviation in the nerve trunks. In the

same child there were many hernias in the skull, with no bone formation in these areas. The film of the skull showed the usual digital depressions.

OBSERVATIONS ON NEW-BORN INFANTS. Presented by DR. A. LEVINSON.

Lantern slides illustrating the following conditions were shown: cigaret-paper peeling of the skin, Epstein's pearls and Bednar's aphthae, ichthyosis, physiologic curving of the legs, clubfeet, deformity of the legs due to intra-uterine position, swelling of the eyelids following instillation of silver nitrate, gonorrheal ophthalmia, facial paralysis, missing phalanges, strangulated hernia with sloughing of the scrotum, hydrocephalus and spina bifida, x-ray film of a congenital heart, atelectasis, syphilitic skin lesions and osteochondritis syphilitica.

SICKLE CELL ANEMIA. Presented by DR. MEYER LEVY.

CASE 1.—A colored girl, aged 15 months, was brought to the hospital two months before presentation. The history was that for one month there had been no gain in weight, a diminution in appetite and playfulness, and that for two weeks there had been an abnormal temperature, highest at night. The rest of the history was essentially negative.

Examination on admission showed that the child was poorly developed and undernourished. The temperature was 101 F. The pupils were normal, the conjunctiva pale, the eardrums normal and the tonsils injected and enlarged. There was a slight cervical adenopathy. The heart was enlarged 2 cm. to the right of the sternum and 1.5 cm. to the left of the mammary line. A systolic murmur was present over the apex transmitted to the axilla. The lungs were apparently normal. The abdomen was distended and soft; the liver was enlarged to about three fingerbreadths below the costal margin, and the spleen was enlarged to about the same degree. It was firm, smooth and freely palpable.

The examination of the blood showed: 2,500,000 red cells and hemoglobin, 60 per cent. A stained smear showed anisocytosis, poikilocytosis and nucleated red cells. There was a leukocytosis of 25,000 with 58 per cent lymphocytes, 40 per cent polymorphonuclears and 2 per cent eosinophils.

After three days the temperature became normal and the upper respiratory condition cleared up, but the marked anemia and leukocytosis with predominance of lymphocytes persisted. A roentgenogram of the chest showed the heart enlarged to the right and left, with enlargement about the auricles. The Pirquet, Mantoux and Wassermann tests gave negative results. The fragility tests showed increased resistance of the cells to hypertonic salt solution. Daily blood counts for two weeks showed that the anemia and leukocytosis remained. A splenic puncture was done and the material obtained showed elongated, curved red cells, long sickle cells, many phagocytes and histiocytes.

Attempts were made to treat the blood with many buffer solutions varying from p_H 0.6 to p_H 0.8, and we then obtained sickling. With carbon dioxide sickling occurred, and when oxygen was added the cells regained their normal shape. This has led to the belief that sickling may be due to anoxemia. The frequent occurrence of tuberculosis and heart conditions further substantiates the belief. We were later successful in finding sickle cells in untreated blood smears.

The treatment for this condition is unsatisfactory and everything known has been tried in this case unsuccessfully. At the time of presentation, the hemoglobin was 45 per cent, and the child's general condition had improved somewhat. The radical treatment is splenectomy, and if the anemia continues to increase, that will be done.

THROMBOCYTOPENIA — PURPURA. (TREATED BY SPLENECTOMY.) Presented by DR. J. H. HESS.

A white girl, aged 11 years, was presented because of the response to splenectomy which was similar to that seen in a child, aged 8, whom I presented before this society in April, 1929.

This patient was admitted to the hospital on March 13, 1929. As in the case of the first patient, there was a past history of bleeding. In this case the mother said that the child first showed evidence of repeated skin hemorrhages following minor bruises about one year before. Since that date it had been noted that only slight trauma was necessary to produce a black and blue mark. About three months before admission the child had a molar tooth extracted followed by hemorrhage for two days. The mother also said that during the past three months she noticed that the child's gums bled readily and that she had frequent attacks of epistaxis; for five days before admission the attack had been almost continuous. No blood had been observed in the urine or stools. She has not menstruated.

Observations

	Before Splenectomy							
	3/14	3/20	3/27	4/5	4/12	4/20	4/26	5/3
Bleeding time (Duke)	46 min.	54 min.	53 min.	32 min.	56 min.	54 min.	60 min. +	4 min.
Clotting time (Howell)	11 min.	10 min.	10 min.	8 min.	12 min.	11 min.	12 min.	2½ min.
Clot retraction	None in 48 hours	None in 48 hours	None in 48 hours	None in 24 hours; retraction in 48 hours	None in 48 hours	None in 48 hours	None in 48 hours	Good in 2½ hours
Platelet count	10,000	18,000	12,000	20,000	30,000	40,000	80,000	470,000
Platelet function	Few fibrin threads but of good quality	Scant amount of fibrin of good quality formed in 18 min.	Few fibrin threads	Fibrin of good quality in 15 min.	Scant amount of fibrin	Good fibrin threads in 15 min.	Good fibrin formation in 17 min.	Good fibrin in 11 min.
Turniquet test	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Negative for 5 min.
Hemoglobin (Newcomer)	42%	40%	39%	44%	41%	45%	44%	48%
Red blood cells	2,800,000	2,950,000	2,750,000	3,050,000	2,960,000	3,250,000	3,100,000	3,250,000
White blood cells	12,400	14,100	14,400	13,100	15,000	12,000	13,600	12,100
Differential count, per cent (500 cells)	P.....83 L..... 9 M..... 3.7 E..... 2 B..... 0.25	P.....81 L.....10 M..... 6 E..... 2 T..... 1	P.....78 L.....14 M..... 5 E..... 3	P.....80 L.....10 M..... 7 E..... 2.5 T..... 0.5	P.....82 L.....10 M..... 7 E..... 1 T..... 0.5 B..... 0.5	P.....81 L..... 7 M..... 8 E..... 3 B..... 1	P.....79 L.....14.25 M..... 4.7 E..... 1.5 B..... 1	P.....84 L..... 8 M..... 7 E..... 1

There was nothing of importance in the medical history except that the patient was subject to "sinking spells," growing weak and frequently vomiting during these attacks, but with no loss of consciousness.

The results of the physical examination were negative, except for numerous ecchymotic areas. There were two petechial hemorrhages on the soft palate. The teeth were in good condition. The tonsils presented nothing abnormal. The margins of the gums were swollen and hemorrhagic; blood was present in the nostrils. The anterior and posterior lymph nodes were considerably enlarged.

The heart showed moderate hypertrophy and there was a systolic murmur, probably organic. The liver and kidneys were not palpable. The spleen was moderately enlarged on the first examination and gradually increased in size with soft consistency. Many petechial spots and ecchymoses were present on all the extremities and also on the neck. These varied from 0.5 to 1.5 cm. in diameter.

The clinical diagnosis was mitral regurgitation, rheumatic endocarditis and secondary purpura hemorrhagica.

During her stay in the hospital, covering about six weeks, the patient had a low grade, irregular temperature, which ranged most of the time from normal

to 101.5 F. Occasionally there were more marked excursions. At times during the early weeks in the hospital she showed macroscopic blood in the stools and urine. The Wassermann reaction was negative.

Various therapeutic measures were undertaken, including the administration of large doses of calcium lactate, wheatamin, liver extract, horse serum and whole blood intramuscularly, and exposure to ultraviolet light. None of these seemed appreciably to improve her condition.

After forty-eight days on the medical service she was transferred to the surgical department for splenectomy. At the time of operation the spleen measured 11.5 by 6 by 2.5 cm. Sixteen days after splenectomy she was returned to the medical service and left the hospital on the twenty-fourth day after operation.

on the Blood

	After Splenectomy, 4/30					After Discharge			
5/5	5/9	5/12	5/16	5/19	5/23	6/20	7/28	8/19	9/14
15 min.	8 min.	10 min.	14 min.	10 min.	9 min.	4 min.	6½ min.	5 min.	5½ min.
7 min.	6 min.	5½ min.	5½ min.	7 min.	6 min.	8 min.	5 min.	4 min.	6 min.
Fair in 24 hours	Good in 24 hours	Good in 8 hours	Good in 12 hours	Good in 12 hours	Good in 12 hours	6 hours	1½ hours	3 hours	2½ hours
200,000	250,000	240,000	180,000	190,000	160,000	150,000	130,000	190,000	210,000
Fibrin formation in 19 min.	Good fibrin in 14 min.	Good fibrin in 12 min.	Good fibrin in 15 min.	Good fibrin in 14 min.	Good fibrin in 20 min.	Good fibrin in 18 min.	Good fibrin in 12 min.	Good fibrin in 19 min.	Good fibrin in 14 min.
Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative
47%	49%	52%	55%	54%	54%	60%	54.5%	61%	67%
3,150 000	3,060,000	3,160,000	2,390,000	2,680,000	3,204,000	3,750,000	4,450,000	4,540,000	4,250,000
11,500	10,800	12,000	12,500	9,900	10,000	11,200	10,600	12,100	9,800
P.... ..82 L.....12 M..... 4.5 E..... 0.5 Marked reticulocytosis (vital stain)	P.....81 L.....12 M..... 6 E..... 0.5 T..... 0.5	P.....89 L..... 8 M..... 2 E..... 1	P.....80 L.....14 M..... 5 E..... 1	P.....77 L.....15 M..... 7 E..... 0.5	P.....75 L.....20 M..... 3 E..... 2	P.....68 L.....22 M..... 7 E..... 3	P.....65 L.....28 M..... 4 E..... 3	P.....68 L.....20 M..... 8 E..... 4	P.....60 L.....17 M..... 8 E..... 4 T..... 1

At the time of operation she received 250 cc. of blood intravenously. She vomited some blood-containing material the first three days following operation. On the fifth day her condition was reported as good. She was up and about in a wheel chair on the eleventh day.

On Nov. 19, 1929, the blood showed: hemoglobin (Newcomer) 75 per cent; red cells, 4,540,000; white cells, 9,400; platelets, 243,000; bleeding time, two and one-half minutes; platelet function, six and one-half minutes; coagulation time, thirteen minutes; clot retraction began in two hours, completed in five hours; tourniquet test, negative at end of ten minutes; differential count: red cells, normal; white cells: polymorphonuclears, 50 per cent; lymphocytes, 31 per cent; monocytes, 8 per cent; eosinophils, 10 per cent; basophils, 1 per cent; 300 cells were counted.

DISCUSSION

DR. EDWIN M. MILLER: This is the only case of this kind with which I have had any experience. From a résumé of the literature, it appears to me that if a diagnosis of thrombocytopenic purpura is made and the condition is not

due to defective formation of the blood platelets on the part of the bone-marrow, removal of the spleen not only is indicated, but is very apt to be followed by a favorable result. In 80 per cent of the reported cases the outcome has been satisfactory, but the mortality has ranged around from 8 to 10 per cent. It is not a simple matter to subject a child who bleeds so easily to a splenectomy; a blood transfusion done at the same time may be the deciding factor in the recovery. I have found recently a report in the Belgian literature to the effect that ligation of the splenic artery has been done in place of removal of the spleen, with favorable results in a small series of cases. The mortality is lower than that for removal of the spleen. The result after ligation, I presume, may be considered just as effective as actual removal of the organ, although there are not enough cases on record to permit drawing definite conclusions. If it proves of value, we may consider substituting it for splenectomy.

VAGINITIS IN CHILDREN (TREATMENT). Presented by DR. RUSSELL D. HERROLD.

Several months previously I became interested in the treatment for vulvovaginitis in children, and with the cooperation of Dr. Blatt and his staff I felt that perhaps we might get somewhere with the treatment for this very resistant disease.

The criterion of results depends on the duration of time that these patients remain gonococcus-free and the interpretation of treatment must depend on such observations. Any evaluation of results must be guarded for we have all seen exacerbations after clinical quiescence for months and years.

I believe that there is a distinct similarity in many ways between infections in children and those in adults. There are fewer complications in children although arthritis is rather common. In the chronic stage of infection the condition is similar to a like chronicity in adults. The children may be clinically free, with the smears negative over long periods, and then for some reason, perhaps a decreased resistance of the body, there is an acute exacerbation. It seems to me that treatment for the eradication of the gonococcus must be directed toward the means of increasing the resistance of the body. Many instances of spontaneous cure of gonorrheal infections are known. Valuable observations could be made if it were known why one patient will become bacteriologically free from gonococci and another on the same management will remain positive for the gonococcus.

One phase of our work has been an attempt to evaluate the use of biologic serums. An antihorse serum has been produced in the usual way except the antigen consisted of both exotoxic and endotoxic products. The gonotoxin is distinctly different from the toxins produced by diphtheria especially as manifested by reactions in both animals and human beings. In general these reactions are similar to those described with toxins of hemolytic streptococci and *Staphylococcus aureus*. There is no definite standardization of the potency of gonococcus antiserum by laboratory titration. Our only criterion was the neutralization of toxin by properly controlled skin reactions in human beings and the presence of agglutinins in dilution of the serum 1:400 or higher. Most of the serum was concentrated by the Felton method before use. Many of the patients had a mild local reaction but few had general reactions. It is too early to give any definite interpretation of the results.

We believe that it is also worth while to attempt a more accurate evaluation of vaccine therapy. Emphasis is being placed here on the determination of the best type of vaccine or antigen to use and the best method of giving it. This includes the optimum interval between injections and the relative efficiency of intracutaneous, subcutaneous and intramuscular injections. Ecto-antigens, autolysed extracts of whole bacteria and detoxicated vaccines are the more common types in general use. Many immunologists are getting away from the old ideas of antibody production, and the trend is toward the view that the specific antibodies are the retained products of the altered antigen, whether derived from the infection

itself or from the injected vaccine. This opens up a new field for the production of antibodies, not only in vivo but possibly in vitro.

There is no doubt that antiseptic treatment has some value, particularly the newer methods requiring the use of such drugs as mercurochrome-220 soluble in petrolatum and hydrous wool fat or acriflavine in gelatin, but it would seem that the ultimate control of the disease must come through specific biologic products or chemical therapeutic measures.

ROENTGENOGRAPHIC STUDY OF SYPHILITIC BONE LESIONS IN NEW-BORN INFANTS. Presented by DR. PARMELEE.

During an investigation of infants born of syphilitic mothers, Dr. Halpern and I have gone over carefully a rather large number of roentgenograms and a few observations, which are really by-products of our main theme, seemed of enough interest to warrant bringing them to your attention briefly.

1. The similarity of the roentgenographic observations at the ends of long bones in scurvy and in syphilitic osteochondritis; that is, the widened epiphyseal line and the area of decreased density in the metaphysis immediately proximal to the epiphyseal line. There are, of course, differential points, which when sufficiently evident will prevent confusion, for example: in syphilitic osteochondritis the distal margin of the epiphyseal line is irregularly serrated, the spongiosa is moth-eaten in appearance, often in striking contrast to its smooth, ground-glass appearance in scurvy. Also, when periosteitis is present, it can usually be easily distinguished from the picture of the periosteum lifted away from the shaft as seen in scurvy.

2. Scurvy and syphilis may be present in the same person, and the roentgenologic observations may be a compound picture produced by these pathogenic agents. In such a case it is difficult to determine which change is produced by one and which by the other.

3. Periosteitis is not usually recognizable as early as osteochondritis for the reason that it must be thick enough, or calcified enough to cast a shadow, before it can be recognized. The widened zone of preliminary cartilage calcification with the trümmerfeldt zone proximal to it are early changes both in scurvy and in syphilis, and are usually recognizable several weeks before scurvy or periosteitis can be made out in syphilis.

The following prenatal records and notes from the cases studied will serve to illustrate these points.

CASE 1.—On Dec. 31, 1928, the mother's Wassermann reaction was 4+. She received six injections of neoarsphenamine altogether at the Chicago Lying-In Hospital and also mercury and potassium iodide for one month.

The baby was born on March 15, 1929. He was seen at 3½, 6 and 7 months and at each examination seemed normal. Roentgenograms were taken at 7 months and showed observations suggestive of either scurvy or syphilis; more likely scurvy because of the absence of symptoms and negative serologic observations at each examination.

CASE 2.—In September, 1929, the mother's Wassermann reaction was 4+. She received one injection of neoarsphenamine, with no other treatment. She was a tripara; the first child died at the age of 9 months, cause unknown. The second child was premature at 8 months; it died soon after birth.

The third child was born on Oct. 5, 1928. She weighed less than 5 pounds (2,267.96 Gm.). At birth the spleen was definitely palpable. There were no snuffles, maceration or eruption; all other observations were negative. At 6 weeks the baby was very puny and had bloody discharge from the nostrils. She died at 8 weeks, cause unknown.

At 3 days and 6 weeks, the Kahn and Wassermann tests both gave 4+ reactions. Roentgenograms showed epiphysitis in the first film and epiphysitis and periosteitis in the second.

CASE 3.—The mother's Wassermann reaction was 4+. On Nov. 28, 1928, she received one injection. No other treatment was given.

The baby was born on December 9. It was underweight, but there was no sign of syphilis. The baby was put on treatment and was admitted to the hospital at 3 months. At 2 days and at 3 months, the Wassermann and the Kahn reactions were 4+. A roentgenogram taken in the first week showed characteristic epiphyses but no periosteitis. At 3 months osteochondritis and periosteities were present. There was an irregular moth-eaten appearance of spongiosa in contrast to the ground-glass appearance of scurvy.

CASE 4.—The mother's Wassermann reaction was 4+ on Feb. 25, 1929. It was her second pregnancy. The other child was normal. Treatment was started in February, 1929.

The baby was born on May 10; it weighed 7¾ pounds (3,515.4 Gm.). All the observations were normal in the hospital and at 6 weeks, except on the latter date the tip of the spleen was palpable.

The Wassermann and Kahn tests gave negative results on the fifth day and at 6 weeks. A roentgenogram taken on May 15 showed: the epiphysis was thick, with a rarefied area proximal to it. On June 25, the foregoing observations were somewhat more pronounced.

CASE 5.—The mother's Wassermann reaction was 3+ on Oct. 12, 1928. She received one injection of neoarsphenamine. She had one child living and well. There had been no miscarriages or stillbirths.

The baby was born on Jan. 8, 1929. The observations were normal the first week, and at 6 weeks, 3 months and 6 months.

The roentgenologic observations were not abnormal until 6½ months. There was a thick, not irregular, epiphyseal line. A ground-glass appearance of spongiosa was present, with no evidence of bone destruction, signifying scurvy.

CASE 6.—The mother's Wassermann reaction was 4+ on Dec. 5, 1928. She received two injections of neoarsphenamine.

The baby was born on Feb. 8, 1929. The birth weight was 4 pounds 14 ounces (2,211.27 Gm.). The baby was one month premature.

Observations were: fourth day, no suggestion of syphilis; six weeks, undernourished, palms and soles shiny, no eruption, no snuffles, put on treatment; three months, improved greatly, spleen palpable; six months, improved condition, weight 10 pounds (4,535.92 Gm.), spleen palpable.

The roentgenologic observations resembled those of rickets more than those of syphilis, but the calcification at the epiphyses was not characteristic. There was a combination of syphilis and rickets.

PROGNOSIS OF TETANUS. Presented by JOSEPH K. CALVIN.

The results in 183 cases of tetanus, in which treatment was given at the Cook County Hospital during the past thirteen years, are here summarized. The mortality varied from 27 to 82 per cent per year. There was no tendency toward a diminishing mortality in the later years. The mortality according to age indicates that the highest mortality was between 1 and 5 years (83 per cent), while the lowest was between 5 and 10 years (34 per cent). In the group of patients from 10 to 15 years of age and in the adults, the average mortality was 65 per cent. The type of injuries that preceded the most fatal forms of tetanus were bullet and powder wounds, the average mortality being 95 per cent and the average incubation period seven days; the least fatal were lacerations, with a mortality of 44 per cent, and an incubation period of twelve days; in splinter wounds the mortality was 41 per cent, and in postoperative cases, 45 per cent. It is of interest that in three cases of frozen feet in which tetanus developed the mortality was 100 per cent. In cases of tetanus developing from nail wounds, a common type of injury, the mortality was 66 per cent. In five cases of tetanus after burns, the mortality was 80 per cent. The greatest number of cases followed lacerations, the mortality being only 44 per cent and the average incubation period twelve days. The relation of mortality to

the site of the injury in our series reveals that patients with face and head injuries, per se, do not necessarily develop a more fatal form of tetanus, the mortality in fourteen cases being 50 per cent and the average incubation period twenty-one days, while patients with arm and leg injuries averaged nearer 61 per cent, with an average incubation period of ten days. Apparently, the most important factor in the prognosis of tetanus is the length of the incubation period. Specific therapy has not altered this fact. In cases with an incubation period under ten days, the mortality is around 84 per cent whereas in cases with an incubation period between fourteen and twenty-one days the mortality is 25 per cent. The duration of the disease after it is established is of extreme importance in the prognosis. If the patient lives ten days, he has an even chance to recover. The greatest number of deaths occur within the first three days of the disease with a rapid decrease in the ultimate mortality in those surviving the first three or four days.

RHEUMATIC INFECTIONS (TREATMENT). Presented by DR. IRISH.

CASE 1.—A girl was admitted to the hospital on October 29 with an acute case of chorea. She had been sick for one week. Her temperature on admission was 101 F., and it ranged up and down until the fifth day in the hospital, when it reached a little above 103 F. Coincident with the development of this high temperature, I found a pericardial rub which had not been present before.

During the first five days, she received large doses of salicylates, 20 grains (1.3 Gm.) three times a day, combined with 20 grains (1.3 Gm.) of sodium bicarbonate, also three times a day. We then changed the medication to cinchophen, 30 grains (1.95 Gm.) a day. Her temperature rose to 104 F. that night and then started to drop, and remained normal since that time. The pericardial rub persisted for about a week, but there was immediate relief from the fever and marked coincident improvement in the pain. A striking feature was the rapid clearing up of the chorea. I never saw such a violent case subside in eight days as this one did.

CASE 2.—A girl was admitted to the hospital on October 19, with a history of rheumatism of three weeks' duration and shortness of breath. Examination revealed an inflamed hypertrophy of the tonsils and a definite mitral murmur. No pericardial rub could be elicited. Her temperature on admittance was 102 F., and it varied between 101 and 105 F., which was reached on the fifth day.

During this period, she was given large doses of salicylates, almost 100 grains (6.5 Gm.) a day, and we then started doses of cinchophen. The temperature was then 103 F. On the following day it rose to 104 F., after which it dropped and since remained normal, or nearly so. Coincidentally, there had been clinical improvement in all the other symptoms.

CASE 3.—A boy was presented who had had heart disease. He returned to the hospital with an exacerbation. He had a low fever for about seven days after admission, on large doses of salicylates followed by cinchophen, and his temperature came down to normal in two days and remained so.

CASE 4.—One patient whom I hoped to present made his exit at the end of last week. The boy had been in the hospital since June, 1928. The first period of fever lasted thirty-four days, and he was given salicylates in fairly large doses. His fever came down, so that the temperature was about 102 F. He was then given cinchophen, and the temperature became normal in two days and remained so for about thirty days. During fifteen days of this time, he received cinchophen. He was again given sodium salicylate but proved resistant and the dose was again changed to cinchophen. He showed all the signs of a protracted, active rheumatism, with a special tendency toward the exacerbation of cutaneous symptoms. At various times he showed every possible rheumatic skin manifestation. At no time during the year and a half of his illness while he was receiving cinchophen did he develop an exacerbation of temperature with accompanying symptoms, but he did so when given salicylates and sodium cacodylate, and also when given syrup of iron iodide. The cinchophen seemed to be efficient in preventing a return of the febrile manifestations while he was taking it, but it was not sufficient to prevent a return of symptoms when the use was discontinued.

CASE 5.—A colored girl entered the hospital on November 4, with an outside diagnosis of acute peritonitis, and a temperature of 102 F. The diagnosis made in the examining room was acute gastro-enteritis. I saw her on the first morning and detected a distinct pericardial rub. We decided not to have her operated on and gave her salicylates, 60 grains (3.9 Gm.) in twenty-four hours. The next morning her "surgical belly" had entirely disappeared. The temperature went down on the second day and had not been above 100 F. since then.

The question of the relative efficiency of cinchophen and sodium salicylate has been debated elsewhere. Probably the cinchophen group has not been used so much in children as in adults, because it is not so easy of administration. It is practically insoluble in water, as is neocinchophen. It can be given in capsules to older children and put in powders with powdered cocoa and sugar for younger children.

I believe that some early cases are apparently salicylate resistant, and some of the late cases are probably salicylate-fast. A change to one of the cinchophen group is indicated when one does not get rather prompt results with salicylates. I believe that cinchophen is a more potent analgesic than salicylate, that it causes less irritation of the stomach and that exacerbations are less frequent under this drug.

Our initial dosage for salicylates is 1 grain (0.065 Gm.) to the pound of body weight the first twenty-four hours and 1½ grains (0.097 Gm.) for cinchophen, diminishing as improvement occurs. Alkalis should be used with the cinchophen group although they were omitted in these cases for observational reasons.

NEUROCYTOMA. Presented by DR. LYON.

A colored boy, aged 3 years, entered the hospital on July 22. At that time the mother said that she thought the boy had had a large abdomen all his life but that during the past three weeks it had enlarged quite rapidly, and the child had felt feverish for from three to four weeks. He had complained of a diffuse, cramplike abdominal pain associated with vomiting. The family and past history was negative.

On examination it was found that the patient had a temperature of 100.4 F. The initial and the essential symptoms were in the abdomen, which the intern described as being "pot like." In addition, there was a nodular, irregular mass extending down to the umbilicus, which was interpreted as the liver. There was some crepitation over this mass, which was thought to be bowel. In the upper left quadrant there was a mass which resembled the spleen. In the left axilla the lymph nodes were enlarged. Physical examination was otherwise negative.

The conditions considered from the start were: a probably retroperitoneal malignancy with metastasis to the liver; miliary tuberculosis involving the spleen and liver. Congenital syphilis had to be excluded, and Gaucher's and Pick's anemia also had to be considered.

The blood showed: 3,000,000 red cells, 6,400 white cells and hemoglobin 70 per cent. The differential count was within relatively normal limits. The urinalysis and the chemical analysis of the blood gave negative results, as did the Pirquet and Mantoux tests. Roentgenologic examination of the chest revealed observations that led the roentgenologist to report "diffuse consolidation about the hilus, suspicious of tuberculosis." A barium enema revealed displacement of the hepatic flexure of the transverse colon median downward. This was interpreted as a displaced loop of bowel as the result of a tumor in the upper right quadrant. Splenic puncture was seriously contemplated, but there was some doubt as to whether the tumor was actually on the spleen.

The patient's course was steadily downward, the abdominal distention increased and he was apparently in considerable pain. Three days after admission a biopsy was performed on an axillary lymph node. Later an exploratory laparotomy was done by Dr. E. M. Miller, and a large liver filled with metastases was found, with a tumor in the region of the right kidney. The mass that had been looked on as possibly the spleen was the left lobe of the liver. The child did not rally following the operation and died during the afternoon.

At necropsy, when the abdomen was opened it was found that in the right suprarenal body there was a large, ovoid mass, approximately 10 by 15 cm., which included only the right suprarenal body. The liver reached 15 cm. below the xiphoid, and weighed 1,820 Gm. There were large yellow and gray metastatic nodules. In addition to the metastasis to the liver, it had also involved the sixth and seventh intercostal regions, with definite erosion. A group of glands in the axilla was definitely gray and somewhat soft and there was also some tumor formation. Professor Jaffe examined the skull carefully and was greatly interested to find evidence of one of the metastases in that region. The pathologic diagnosis of neurocytoma was made by him.

THYROTOXICOSIS. Presented by DR. PHILIP ROSENBLUM.

In recent years there has been a great increase in the number of cases of exophthalmic goiter that have been reported, and many more patients have been operated on than ever before. Recently there seems to have been an increase of the number of cases occurring in childhood, and more have been seen here during the past two or three years than ever before. Formerly this disease was rarely seen in children. In 1922, a survey in Switzerland showed only five cases in children between 7 and 10 years of age.

CASE 1.—A girl, aged 11, was admitted to the hospital early in November, with a history that for eight months she had been extremely nervous. She had attacks of staring, with marked bulging of the eyes, and complained of "pounding" in her heart. She presented a well developed case of exophthalmic goiter almost as well developed as in an adult. The eyes protruded, the goiter was quite evident, she had a fine tremor, the pulse rate ranged between 120 and 150 and she had a slight elevation of temperature. Her blood pressure was 140 systolic and 72 diastolic, with a very high pulse pressure. The basal metabolic rate was plus 15.

The basal metabolism in this type of case has not been worked out to the degree it has in the adult because of the rarity of the cases. In other cases the basal metabolism has been out of proportion to the clinical observations; that is, lower than one would expect. In another case there were all the evidences of exophthalmic goiter: protrusion of the eyeballs, a pulse rate of from 150 to 160 and a basal metabolic rate of plus 25 only, so that there is a question of the relative value of the basal metabolism test in exophthalmic goiter in childhood. When enough cases are worked up it may be found that the rate is not as high in childhood as in adults with corresponding symptoms and signs.

The question comes up as to whether the increase in cases of exophthalmic goiter in childhood might not be related to the use of iodized salt, as is claimed in some adult cases. This patient had used iodized salt for two years.

Most of these cases in childhood have occurred in girls. The treatment is important, and I think that not many pediatricians know much about it, because they see so few cases. The patient I just presented has greatly enlarged tonsils and two badly infected teeth. In the light of some recent work from Dr. Lahey and others, we feel that she should be given the benefit of medical treatment for a longer period. It has been taught recently that we should not give iodine over a long period in cases of exophthalmic goiter, except just before operation, but it has been shown in the East that by giving iodine over long periods physicians have been able to cure patients with thyrotoxicosis without operation. We feel that in this case the diseased tonsils and teeth should be removed, and that the child should be put at rest in bed and given iodine over a long period as she may be benefited by these measures.

HEREDITARY SYPHILIS. Presented by DR. BLATT.

There has been a general tendency in this department during the past few years to treat patients with hereditary syphilis by means of arsenicals. I have discarded this treatment recently and have reverted to the use of mercurial inunctions. I am using 10 per cent unguentum hydrargari, 1 Gm. every second day,

applied to paraffin paper and inverted on the body, varying the site from day to day. The child is bathed before each succeeding application. The thought that in syphilis more than in any other disease, the patient and not the disease must be treated, has compelled me to make the change. Our results with the arsenicals showed a large number of fatalities in the frail infants entrusted to us. We believe that we are making a latent syphilis out of an active one. In this condition, the child continues to grow and develop under the usual dietetic handling. The Wassermann reaction remains positive. It is our plan to use the arsenicals when the child has sufficient resistance to tolerate these drugs.

CASE 1.—Dolores Wilson was admitted to the hospital on May 25, 1929, weighing 7¾ pounds (3,515.4 Gm.). She was poorly nourished and had rhagades about the mouth and a free nasal discharge. The plantar surfaces of her feet were scaly. The Wassermann reaction was 4 plus. Three weeks from the time mercurial treatment was begun the skin was clear and the weight chart assumed the normal curve.

CASE 2.—Ardley France was admitted to the hospital in September, 1929, at the age of 10 weeks, weighing 8 pounds (3,628.74 Gm.). The mother had received weekly antisyphilitic treatment during pregnancy. The infant showed exfoliation of the palms and soles, a palpable spleen and a 4 plus Wassermann reaction. The spleen was somewhat larger than at the time of entrance but the infant's gain in weight had continued steadily since treatment was begun.

CASE 3.—Edgar Bradford was admitted to the hospital in June, 1929, with a diagnosis of malnutrition. He had not gained weight during the preceding month, and had a papular eruption on the scalp and chest. Desquamation of the palms had been present since birth. The mother had been treated for syphilis during pregnancy and in July the Wassermann reaction was twice negative. The child's liver and spleen were palpable and he had a 4 plus Wassermann reaction. The rate of gain had been slow but steady.

CASE 4.—Herbert West was admitted to the hospital on Oct. 24, 1929, at the age of 6 weeks. He showed an irregular, generalized, macular, scaly eruption, a generalized lymph adenopathy and a palpable spleen. The Wassermann reaction was 4 plus. His eruption had cleared, his snuffles had lessened, his spleen was no longer palpable and he was gaining weight. His mother had received seven injections during pregnancy.

CASE 5.—The mother of this patient had taken antisyphilitic treatment at irregular intervals. M., aged 8, showed her first symptoms two years before presentation. An injury to the lip failed to heal. From time to time during the last two years ulcerative lesions had appeared elsewhere on the body. They had tended to heal, but broke down again. Scars from these lesions were seen on her hands, over both ulna and over the malleoli. On entrance to the hospital she showed ulcerative lesions with osteomyelitis of the left tibia, of the right ulna and of one of the metacarpal bones. She had been treated with 10 per cent mercurial ointment, applied to the open lesions and had had a total of 3.15 Gm. of sulpharsphenamine, during the past five weeks. The lesions were rapidly healing and new bone, apparently perfectly normal, was replacing the osteomyelitic portion. The urine had been normal throughout and she had shown no evidence of unfavorable reaction to the drugs.

Book Reviews

THE PHYSIOLOGY OF ORAL HYGIENE AND RECENT RESEARCH. By J. SIM WALLACE, D.Sc., M.D., L.D.S. (London). Price, 10 shillings, 6 pence. Pp. 228, with 7 illustrations. London: Baillière, Tindall & Cox.

This book of twelve chapters (with seven illustrations) is essentially a grouping of lectures delivered by Dr. Wallace on various occasions before British and American Dental Societies and college students. The various chapters are skilful, forceful and repeated expositions of the author's ideas regarding the cause of dental caries, the comparative value of research in this field by various investigators and methods available in preventing dental disease.

He emphatically questions the importance of vitamin deficiency in the diet as a factor in susceptibility to caries, and presents many good arguments in refutation of the theories of susceptibility so frequently promulgated by dietary investigators.

Dietary habits, rather than the chemical constituents of foods, are the suggested cause of dental caries, and the author would prevent it by education in avoiding soft, mushy and starchy foods, especially the carbohydrates, and finish each meal with a food that would cleanse the teeth, carrying away the carbohydrate accumulations from the retentive spaces about the teeth.

The ideas presented are well worth studying, although the material could easily have been condensed to one-half its volume by elimination of useless repetition and frequent vigorous attacks on research workers not in agreement with his views.

The bibliography is complete, and the entire work shows a thorough and careful investigation of the subject presented. While many men will be in disagreement with the facts Wallace presents, the book undoubtedly warrants a thorough study and serious consideration by those interested in promoting the dental health of children individually or collectively.

DIE SÄUGLINGSERNÄHRUNG. By L. F. MEYER and E. NASSAU. Price, 25 marks. Pp. 353, with 85 illustrations. Munich: J. F. Bergmann, 1930.

When one takes up this book he is struck in looking through it by the painstaking and methodical way in which the subject is treated. The book is not exhaustive, nor is it intended to be, but there is sufficient data to cover all the points that are necessary for the practical consideration of the subject.

The preliminary chapters on the physiology of the infant and on milk with digestion and metabolism are well considered and adequately treated. Breast feeding is considered in detail. The material on artificial feeding of the healthy child is most enlightening in view of the distorted ideas that some American students seem to have brought back from Germany. The ideas conform closely to those held by conservative pediatricians in this country. There is a chapter on the nourishment of the premature and debilitated child which is well worth reading. Possibly no part of the book, however, is better than their consideration of the pathology of nutrition in infancy. When it comes to disturbances of nourishment, they speak of three groups: eutrophy, dystrophy and atrophy. They then feel that each of the two latter categories must be considered as to whether they are produced by: (1) diarrheal disturbances, (2) infection, (3) discrepancies in nutrition or (4) abnormal constitution. The avitaminoses and constitutional diatheses are well presented, as are the so-called secondary alimentary disturbances in which are included rickets, tetany and the anemias.

No attempt is made in this volume to supply a bibliography. Authors are cited, but the reference is not given. The book should, however, prove an excellent general basis for the subject and goes much more deeply into the scientific end than do any American books as yet published.

DIE BEHANDLUNG UND VERHÜTUNG DER RACHITIS UND TETANIE. By P. GYORGY. Price, 9.60 Rm. Pp. 221, with 31 illustrations. Berlin: Julius Springer, 1929.

This monograph is the reproduction of a review which appeared in a recent number of the *Ergebnisse der inneren Medizin und Kinderheilkunde*, vol. 36. It is a careful consideration of the subject by one who for many years has been actively engaged in its investigation, both in the laboratory and in the clinic. It considers not only the prophylactic and curative treatment for rickets and tetany, but also its diagnosis, etiology and pathogenesis. The bibliography is exceptionally full, including more than 1,500 references. The monograph can be recommended to all who wish to read or refer to an account that comprises the newer points of view of rickets and tetany. The indications for direct and indirect irradiation therapy are carefully outlined, and the question of "hypervitaminosis" is adequately discussed.

POSTURE AND HYGIENE OF THE FEET. By PHILIP LEWIN, M.D. Price, 30 cents. Pp. 47, with 25 illustrations. New York: Funk & Wagnalls Company, 1929.

This is a well written booklet, which can be understood by lay people. It contains many illustrations of the more common conditions, which are self-explanatory. Considering the size of the volume, many of the ordinary disabilities of the feet are thoroughly discussed in simple terms.

The most important phase of the work throughout the volume is prophylaxis, in that the author emphasizes and constantly gives specific directions for the prevention of minor foot troubles.

Directory of Pediatric Societies

INTERNATIONAL

International Pediatric Congress

Prof. I. Jundell, Artillerigatan 23, Stockholm, Sweden.
Place: Stockholm. Time: Aug. 17-20, 1930.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. William Weston, 1231 Bull. St., Columbia, S. C.
Secretary: Dr. C. A. Aldrich, 545 Lincoln Ave., Winnetka, Ill.
Place: Detroit. Time: June 23-27, 1930.

American Child Health Association

President: Hon. Herbert Hoover, 370 7th Ave., New York.
Secretary: Dr. Philip Van Ingen, 370 7th Ave., New York.
Place: Fort Worth, Texas. Time: October, 1930.

American Pediatric Society

President: Dr. Joseph Brennemann, 30 N. Michigan Blvd., Chicago.
Secretary-Treasurer: Dr. Howard Childs Carpenter, 1805 Spruce St., Philadelphia.
Place: Windsor Hotel, Montreal. Time: June 17-19, 1930.

Association of American Teachers of the Diseases of Children

President: Dr. Lawrence T. Royster, State Board of Health, University, Va.
Secretary: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Place: Detroit. Time: June 24, 1930.

Canadian Society for the Study of Diseases of Children

President: Dr. Thomas Crossan Clark, 51 Herkimer St., Hamilton, Ont.
Secretary-Treasurer: Dr. Frank H. Boone, 164 James St. S., Hamilton, Ont.

SECTIONAL

Central States Pediatric Society

President: Dr. Edward Clay Mitchell, 1073 Madison Ave., Memphis, Tenn.
Secretary: Dr. A. H. Parmelee, 310 S. Michigan Blvd., Chicago.
Place: Memphis, Tenn. Time: Fall, 1930.

Southern Medical Association, Section on Pediatrics

Chairman: Dr. H. Leslie Moore, 1717 Pacific Ave., Dallas, Texas.
Secretary: Dr. Ludo von Meysenbug, 3501 Prytania St., New Orleans, La.
Place: Louisville, Ky.: November, 1930.

STATE

Alabama Pediatric Society

President: Dr. J. MacBell, Mobile.
Secretary-Treasurer: Dr. Hughes Kennedy, Jr., Highland Plaza Apts., Birmingham.

Georgia Pediatric Society

President: Dr. W. N. Adkins, Medical Arts Bldg., Atlanta.
Secretary-Treasurer: Dr. E. N. Gleaton, 212 E. Gaston St., Savannah.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. J. A. Crawford, Lake Charles.
Secretary-Treasurer: Dr. C. T. Williams, 7401 Burthe St., New Orleans.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. William M. Taylor, Osler Bldg., Oklahoma City.
Secretary: Dr. Carol Pounders, 110 W. 10th St., Oklahoma City.
Place: Shawnee. Time: May, 1930.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. M. W. Beach, 126 Meeting St., Charleston.
Secretary-Treasurer: Dr. Julian P. Price, The McLeod Infirmary, Florence.

TEXAS PEDIATRIC SOCIETY

President: Dr. H. P. Ledford, 1310 9th St., Wichita.
Secretary-Treasurer: Dr. John G. Young, 3930 McKinney Ave., Dallas.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. Franklin D. Wilson, 136 York St., Norfolk.
Secretary: Dr. J. B. Stone, 2042 Park Ave., Richmond.

LOCAL

ACADEMY OF MEDICINE OF CLEVELAND, PEDIATRIC SECTION

Chairman: Dr. John Toomey, Cleveland City Hospital, Cleveland.
Secretary: Dr. A. B. Grossman, 7016 Euclid Ave., Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

ACADEMY OF MEDICINE, TORONTO, SECTION OF PEDIATRICS

President: Dr. G. A. Davis, 12 Belsize Drive, Toronto.
Secretary: Dr. Gladys Boyd, 56 DeLisle St., Toronto.
Time: November 17, December 15, February 16 and March 15.

BRONX PEDIATRIC SOCIETY

President: Dr. David I. Frey, 2065 Grand Concourse, New York.
Secretary: Dr. H. M. Eisenoff, 1018 E. 163rd St., New York.
Place: Concourse Plaza, 161st St. and Grand Concourse. Time: Second Wednesday of each month, except June, July, August and September.

BROOKLYN PEDIATRIC SOCIETY

President: Dr. Joseph F. Paulonis, 1357 Bushwick Ave., Brooklyn.
Secretary: Dr. Irwin Schiff, 658 Eastern Parkway, Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Fourth Thursday of October, January and April.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Arthur H. Parmelee, 310 S. Michigan Blvd., Chicago.
Secretary: Dr. Bert I. Beverly, 130 S. Oak Park Ave., Oak Park, Ill.
Place: City Club. Time: Third Tuesday of each month.

Detroit Pediatric Society

President: Dr. Wyman C. C. Cole, 2970 W. Grand Blvd., Detroit.
Secretary: Dr. Charles A. Wilson, 71 E. Perry St., Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. Lee Bivings, Exchange Bldg., Atlanta.
Secretary: Dr. William Kiser, Medical Arts Bldg., Atlanta.
Place: Academy of Medicine, 32 Howard St. Time: Second Thursday of each month from October to April, 8 p. m.

Memphis Pediatric Society

President: Dr. G. J. Levy, 899 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. W. R. Graves, 1024 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

Milwaukee Pediatric Society

President: Dr. M. G. Peterman, 167 17th St., Milwaukee.
Secretary: Dr. F. R. Janney, 418 E. North Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

Nebraska Pediatric Society

President: Dr. H. B. Hamilton, 434 Aquila Court Bldg., Omaha.
Secretary: Dr. George L. Clark, 1817 Vinton St., Omaha.
Place: As announced by committee. Time: Second Thursday of each month from October to June, inclusive, 6 p. m.

New England Pediatric Society

President: Dr. Grover F. Powers, New Haven, Conn.
Secretary: Dr. Gerald Hoeffel, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: October, January and March.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. F. Elmer Johnson, 300 West End Ave., New York.
Secretary: Dr. Hugh Chaplin, 39 E. 75th St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

North Pacific Pediatric Society

President: Dr. W. F. Patrick, Medical Arts Bldg., Portland, Ore.
Secretary: Dr. L. Howard Smith, Medical Arts Bldg., Portland, Ore.

Northern California Pediatric Society

President: Dr. Edward B. Shaw, 384 Post St., San Francisco.
Secretary-Treasurer: Dr. Lloyd Hardgrave, 384 Post St., San Francisco.
Place: Various teaching schools. Time: Monthly.

Northwestern Pediatric Society

President: Dr. C. R. Moriarity, La Salle Bldg., Minneapolis.
Secretary: Dr. E. S. Platou, 730 La Salle Bldg., Minneapolis.
Place: University Campus and Rochester, Minn. Time: Winter, Spring, Summer, Fall.

Philadelphia Pediatric Society

President: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Secretary: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala-Cynwyd, Pa.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

Pittsburgh Pediatric Society

President: Dr. David H. Boyd, 200, 9th St., Pittsburgh.
Secretary: Dr. Theodore C. Elterich, Highland Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months.

Richmond Pediatric Society

President: Dr. Basil B. Jones, 2618 Grove Ave., Richmond, Va.
Secretary-Treasurer: Dr. John S. Weitzel, 3103 W. Franklin St., Richmond, Va.
Place: Westmoreland Club, 601 E. Grace St. Time: First Thursday of each month (other than during the summer).

Rochester Pediatric Society

President: Dr. John Aikman, 184 Alexander St., Rochester, N. Y.
Secretary: Dr. Howard F. Rowley, 278 Alexander St., Rochester, N. Y.
Place: Arranged by program committee. Time: First Friday of each month from October to May.

Rocky Mountain Pediatric Society

President: Dr. Elsie Seelye Pratt, Republic Bldg., Denver.
Secretary-Treasurer: Dr. Wilford W. Barber, Metropolitan Bldg., Denver.
Place: Children's Hospital, Denver. Time: Third Saturday of each month from September to May, inclusive, 2:30 p. m.

St. Louis Pediatric Society

President: Dr. Park J. White, Beaumont Bldg., St. Louis.
Secretary-Treasurer: Dr. Ralph L. Cook, 508 N. Grand Blvd., St. Louis.
Place: St. Louis Children's Hospital. Time: At least once a year and contingent thereafter on the arrangement of a suitable program.

Seattle Pediatric Society

President: Dr. Vernon W. Spickard, Cobb Bldg., Seattle.
Secretary: Dr. Raymond H. Somers, Cobb Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 7 p. m.

Southwestern Pediatric Society

President: Dr. Ezra S. Fish, Pacific Mutual Bldg., Los Angeles.
Secretary: Dr. Fred L. Glascock, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. W. D. Lyon, 101 S. Balch St., Akron, Ohio.
Secretary: Dr. John P. Parsons, 320 S. Division St., Ann Arbor, Mich.
Place: Ann Arbor, Mich. Time: About July 15, 1930.

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